Table 3 – Cancer detection rates in patients undergoing the first transperineal prostate biopsy for 4–10 ng/ml PSA

Author	Patients	Cores (range)	Template	Detection rate
Emiliozzi 2001 [21]	97	12	No	45%
Kojima 2001 [30]	541	12	No	40.8%
Emiliozzi 2003 [10]	70	6TP + 6TR	No	30%
Emiliozzi 2004 [8]	72	12	No	49%
Kawakami 2004 [32]	148	14	No	27%
Furuno 2004 [41]	86	18 (9–33)	Yes	49%
Ficarra 2005 [13]	389	14	No	42.4%
Watanabe 2005 [16]	180	14TP + 12TR	No	33.9%
Yamamoto 2005 [35]	184	12	No	31%

PSA = prostate-specific antigen; TP = transperineal; TR = transrectal.

diagnoses. Such detection rates are usually higher than in transrectal saturation biopsies, reportedly between 13% and 41% [45]. Probably, this might be justified by the higher precision in sampling all prostatic zones and in particular the anterior part of the gland [41].

To date, six studies have compared schemes sampling a different core number, two using different patient samples [8,34] and four using internal controls [13–15,40]. Emiliozzi et al demonstrated an increasing detection rate with higher core numbers, particularly in patients with a PSA of 4–10 ng/ml (30% in 6-core transperineal biopsy vs. 49% in 12-core transperineal biopsy). Pepe et al confirmed these data comparing 12 versus 18 transperineal cores, with detection rates reaching 35% and 51%, respectively [34].

In the studies comparing different schemes through a recursive partitioning within the same patient population, Takenaka et al compared their complete scheme (12 cores) with the standard sextant, obtaining a 20% increase in diagnoses with the additional cores [15]. More detailed studies have been conducted by Ficarra et al in 2005 and by Merrick et al in 2007; both of them confirmed an increase in diagnoses proportional to the increase in core number, reaching 43.8% detection rates in a 14-core first biopsy series [13] and 42.1% in a 24-core repeat biopsy series [40]. These two studies report prostate volume as the strongest predictor for prostate cancer detection [13,40], highlighting the need to increase the number of cores in prostates $>$ 50 cc [13].

Another variable to be taken into account for prostate cancer detection is the location of the cores. In studies coming from transrectal biopsy series, prostate cancer has been reported to be located in the peripheral zone in 85% of nonpalpable [46] and in 74% of palpable tumors [47].

On the other hand, transperineal PBx series demonstrate that up to 70% of prostate cancers are located in the anterior part of the prostate [32], with a more frequent involvement of this area in nonpalpable cancers than in palpable ones [32,36] and in repeat biopsy than in the first set [9,41]. Moreover, the transitional zone is involved by cancer in up to 76% of patients with a positive result after a repeat biopsy with a transperineal template approach [31].

With this perspective, prostate sampling should include at least a minimum number of anterior cores in the first set, preferably in the far lateral peripheral zone (anterior horn). According to Ficarra et al, sampling this region with a single core per lobe provides an additional cancer diagnosis in 11% of cases [13].

According to these data, it seems reasonable to deduce that in the first transperineal biopsy setting a minimum of 12 cores should be taken, including the far lateral peripheral zone (anterior horn). Sampling of the transition zone might be omitted in these patients. On the other hand, repeat PBx should include a thorough sampling of the posterior and anterior zones, including transitional cores (Fig. 1). The brachytherapy template in repeat biopsy theoretically provides a more rational prostatic sampling, even though higher anesthetic support is necessary.

3.2.5. *Comparing transperineal and transrectal PBx*

Five studies have been identified comparing transrectal and transperineal PBx, all of them performing transperineal and transrectal PBx on the same patients (Table 4). The first one [7] was a simulation of transperineal (longitudinal) and transrectal (transverse) PBx conducted on radical prostatectomy surgical specimens. In this study, cancer had been initially diagnosed through transrectal biopsy. Nevertheless, 82.5% of the 40 analyzed cancers was redetected by sextant transperineal biopsy, whereas only 72.5% of cases was redetected by transrectal sextant biopsy. These experimental data were confirmed in clinical practice in 2003, when Emiliozzi et al studied 107 patients under-

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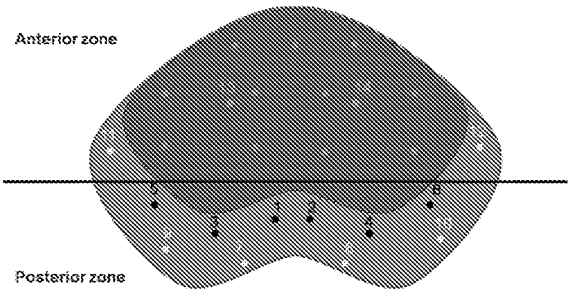


Fig. 1 – Number and location of cores in transperineal prostate biopsy. 1–6 (black) sextant cores; 7–12 (yellow) lateral sextant cores; 13–14 (orange) transition zone cores. Not numbered (pink) cores: possible additional cores in the anterior zone of the prostate.

going 12 biopsies using a combination of the transrectal (6 cores in the peripheral zone) and transperineal (6 cores in the peripheral zone) approach. The authors reported higher detection rates for the transperineal technique. In particular, the study showed an overall cancer detection rate of 40%, with 38% imputable to transperineal 6-core biopsy and 32% due to 6-core transrectal approach. In the subset of patients with a PSA of 4–10 ng/ml, the detection rates of the transperineal and transrectal biopsy were 27% and 20%, respectively [10]. A nearly identical study was performed by Watanabe et al, with different results. In their study, the authors reported an overall detection rate of 48%, significantly lower than the one produced by the six transrectal cores (40%) or by the one produced by the transperineal ones (41.2%). This difference could be due to the different prostatic sampling (6 peripheral transrectal cores versus 4 peripheral and 2 transitional transperineal cores) [16].

A different scenario was proposed by Kawakami et al, one using a systematic transrectal (12 cores) and transperineal (14 cores) prostatic sampling in patients undergoing their first [38,48] or repeated biopsy [14]. In both cases, the route of sampling

Table 4 – Studies comparing transrectal versus transperineal prostate biopsy

Author	Patients	Cores	PSA range	Set	Detection rate (all)	Detection rate (TR)	Detection rate (TP)	*p* (TR vs. TP)	*p* (TP vs. all)
Vis 2000 [7]	40	6TR + 6 TP	NA	NA	NA	72.5%	82.5%	NR	NR
Emiliozzi 2003 [10]	107	6TR + 6TP	4–240	First	40%	32%	38%	0.012	>0.05
Watanabe 2005 [16]	180	6TR + 6TP	4–10	First	48.5%	40%	41.3%	>0.05	0.019
Kawakami 2006 [38]	321	14TP + 12TR	0.9–38	First	34%	21.1%	NR	NR	NR
Kawakami 2007 [14]	235	14TP + 12TR	5.8–12.2 (i.r.)	Repeat	37%	29.3%	30.2%	>0.05	>0.05

PSA = prostate-specific antigen; TP = transperineal; TR = transrectal; NA = not applicable; NR = not reported; i.r.: interquartile range.

Table 5 – Major complications of transperineal prostate biopsy series

Author	Patients	Cores	Set	Severe hematuria	AUR	Fever	Hospitalization
Emiliozzi 2001 [21]	141	12	First	NR	0.7%	0%	0%
Kojima 2001 [30]	679	12	First	2.6%	7.2%	5.2%	NR
Igel 2001 [31]	88	17 T	Repeat	3.4%	2.2%	1.1%	0%
Emiliozzi 2003 [10]	107	6TP + 6TR	First	NR	0%	0%	0%
Novella 2003 [12]	102	14	First	NR	3%	1%	0%
Emiliozzi 2004 [8]	107	12	First	NR	0%	0%	0%
Kawakami 2004 [32]	289	14	First	1%	0%	0%	1.4%
Buskirk 2004 [49]	157	12	First	NR	11%	NR	NR
Furuno 2004 [41]	113	18 T	Mix	NR	1%	0%	0%
Ficarra 2005 [13]	480	14	First	0.4%	0.6%	0.6%	0.6%
Pepe 2005 [34]	372	18	NR	NR	4.3%	0.8%	NR
Watanabe 2005 [16]	402	6TR + 6TP	First	0.5%	0.5%	0.5%	NR
Bott 2005 [33]	60	24 T	Repeat	2%	NR	NR	NR
Demura 2005 [36]	371	20 T	Repeat	1.6%	1.6%	0%	0
Pinkstaff 2005 [43]	210	21 T	Repeat	NR	11%	NR	NR
Satoh 2005 [9]	128	18 T	Repeat	NR	3.2%	0.8%	0.8%
Kawakami 2006 [38]	321	12TR + 14TP	First	NR	0%	0.6%	0.6%
Moran 2006 [39]	180	41 T	Repeat	NR	10%	NR	NR
Merrick 2007 [40]	102	50 T	Repeat	1%	38%	NR	NR
Kawakami 2007 [14]	235	12TR + 14 TP	Repeat	0.4%	0.4%	0.8%	1.3%

AUR = acute urinary retention; TP = transperineal; TR = transrectal; T = template; NR = not reported; i.r. = interquartile range.

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seems not to affect the ability to detect prostate cancer (88% vs. 88% of the cancers in the first biopsy set and 79% vs. 82% in repeat biopsy), whereas the combination of the two techniques allowed detection of a significantly higher number of cancers, with an overall cancer diagnosis of 34% in case of first biopsy and of 37% in case of repeat biopsy [14,48].

Unfortunately, no study specifically assessed the differences in time consumption and in costs for these two techniques. Nevertheless, because the only differences are in patient preparation and position and the materials to be used are similar, it can be supposed that no substantial differences exist between transrectal and transperineal PBx.

In conclusion, though having a strong rationale, the transperineal approach has not convincingly been demonstrated to provide detection rates higher than transrectal biopsy. High-quality, comparative studies must be performed to assess which kind of biopsy provides better results.

3.3. *Complications*

Most of the series reporting on transperineal PBx provide data concerning the complications related to the procedure. According to those data, transperineal biopsy is a safe procedure. Major complications, such as severe hematuria, acute urinary retention, fever, and other problems requiring hospitalization are rare (Table 5). Considering that in transperineal PBx the needle does not pass through the rectum, fever occurs in 0–1% of cases. Only one series reports fever occurring in 5.2% of cases [30].

Minor complications are more frequent but, because they rarely need treatments, they are seldom reported. In particular, self-limiting hematuria occurs in percentages ranging from 8.6% [34] to 52% [12], hemospermia happens in up to 79% of patients [8], and perineal discomfort or perineal hematoma has lower percentages (1–6%) [12,21]. Unfortunately, only a few authors reported the methods used to collect data concerning complications.

4. Conclusion

Transperineal TRUS-guided PBx is a safe procedure, with high detection rates and low morbidity.

The specific preparation for transperineal biopsy has not been studied through prospective controlled studies. Because the infectious risk of this procedure seems to be low, a single-dose fluoroquinolone prophylaxis has been advised in patients with a standard risk for infection. The execution of a cleansing enema is recommended, and anticoagulant therapy should be stopped only if the hemorrhagic risk exceeds the thrombotic risk.

At least local anesthesia with periprostatic nerve block should be performed. Particularly in repeat PBx or when using the brachytherapy template, some groups propose using spinal or (more rarely) general anesthesia.

Because 6-core schemes provide insufficient detection rates, at least 12 cores are usually taken in the first prostatic sampling. Repeat biopsy, with or without a brachytherapy template, should include more cores, with particular attention to the anterior zone of the prostate.

High-quality, randomized, controlled studies must be performed to support the available evidence that the transperineal approach provides better results than the transrectal one both in terms of complications and results.

Conflicts of interest

The authors have nothing to disclose.

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CME questions

Please visit www.eu-acme.org/europeanurology to answer these CME questions on-line. The CME credits will then be attributed automatically.

1. Transperineal prostate biopsy:
   A. Has to be performed without the guide of transrectal ultrasound (TRUS).
   B. Cannot be performed without general anesthesia.
   C. Has to be performed in selected centers only.
   D. Has to be performed with some kind of anesthesia.

2. In transperineal prostate biopsy, the template technique:
   A. Requires multiple skin accesses and paths to take the cores.
   B. Requires one or two skin accesses for all the cores.
   C. Is the technique of implanting the seeds for brachytherapy at the same moment of prostate biopsy.
   D. Has to be performed with three-dimensional ultrasound equipment.

3. A good-quality first-set transperineal prostate biopsy:
   A. Should include at least six cores.
   B. Should sample the anterior far lateral aspects of the prostate (anterior horn).
   C. Should include at least four cores from the transition zone.
   D. The transition zone should be sampled only for prostate-specific antigen levels > 10 ng/ml.

4. Comparing transperineal versus transrectal prostate biopsy:
   A. There is a theoretical minor risk for infection in transperineal biopsy.
   B. Detection rates are higher in transrectal procedures than in transperineal ones.
   C. Transrectal biopsy requires a more difficult preparation.
   D. Complication rates are higher in transperineal biopsy.

5. To improve detection rates, it is advisable:
   A. To increase the number of cores proportionally to prostate-specific antigen levels.
   B. To decrease the number of cores proportionally to the transition zone volume.
   C. To increase the number of cores proportionally to prostate volume.
   D. To decrease the number of cores in patients undergoing repeat biopsy.

6. In transperineal prostate biopsy, the cleansing enema:
   A. Has the aim to reduce the bacterial load of the rectal mucosa.
   B. Might improve TRUS images and reduce the discomfort during the procedure.
   C. Is contraindicated.
   D. Is rarely performed.

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Interim relief judge
Court The Hague
Doscket number: 619229 / 21-974
Session: 30 November 2021
Date: November 16, 2021

DEED SUBMITTING REACTIVE EXHIBITS

in the case of:

CORBIN CLINICAL RESOURCES LLC, a foreign corporation with its registered office in Cumberland, MD, USA;

plaintiff,

lawyers: S.C. Dack and P. van Schijndel.

versus:

1. Foreign law company **ADVANCE MEDICAL DESIGNS INC**, having its registered office in Marietta, GA, USA;

2. the private company **PELVITEC B.V.**, having its registered office in Delft,

3. **LEAPMED FRANCE SAS**, a company governed by foreign law, having its registered office in Nailloux, France,

4. Mr **NICO EELBODE**,

Defendants,

lawyers: J.J.E. Bremer and A.H. van Duijn

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Corbin submits the following documents by way of deed:

Exhibit 19 Second Expert Report of **Dr. Rick Popert** dated November 15, 2021, with attached:

Exhibit RP-7. *Ultrasound-Guided Biopsy*, chapter from K. Ahrar, S. Gupta, *Percutaneous Image-Guided Biopsy*, Springer 2014

Exhibit 20 **Second W**itness Statement of **Saheed Rashid** dated November 11, 2021, with attachments:

Exhibit SR-7 Homepage Andros Clinics.

Exhibit SR-8 Prof. Debruyne's page on the Andros Clinics website.

Exhibit SR-9 Drs. Jos Immerzeel's page on Andros Clinics website.

Exhibit SR-10 Email dated April 17, 2018 from Mr. Groeskamp to Jos Immerzeel and Rick Popert.

Exhibit SR-11 Email of 12 May 2018 from Jos Immerzeel to Saheed Rashid.

Exhibit SR-12 Email of 5 June 2018 from Jos Immerzeel to Saheed Rashid.

Exhibit SR-13 Email string commencing 22 October 2018 and ending 31 October 2018 between Jos Immerzeel and Saheed Rashid.

Exhibit SR-14E Email string commencing 4 March 2019 and ending 14 June 2019 between Jos Immerzeel and Saheed Rashid.

Exhibit 21 Witness Statement of **Dr. Matthew Allaway** dated November 15, 2021, with the following attachments:

Exhibit MA-1 Ristau et al, *Free-hand transperineal prostate biopsy provides acceptable cancer detection and minimizes risk of infection: evolving experience with a 10-sector template*, Urol Onc 2018, 36(12).

Exhibit MA-2 Emiliozzi et al, *The value of a single biopsy with 12 transperineal cores for detecting prostate cancer in patients with elevated prostate specific antigen,* Journal of Urology Vol. 166, pp. 845-850, September 2001.

Exhibit 22A Email correspondence from 8 to 13 October 2021 between S.C. Dack and MDSS GmbH (AMD's European professional representative for the AMD SureFire Guide).

Exhibit 22B Documents sent by MDSS GmbH on 13 October 2021, including the IFU for the AMD SureFire Guide.

Exhibit 22C Email correspondence from 22 to 28 October 2021 between S.C. Dack and MDSS GmbH.

Exhibit 23 Email dated 12 November 2021 from Philippina Rose of Pelvitec B.V. to b.lugt7@upc.nl, with a flyer for the LeapMed Surefire Guide Kit attached.

Production **24** Dundee PE, Grummet JP, Murphy DG. *Transperineal prostate biopsy: template-guided or freehand?* BJU Int. 2015 May;115(5):681-3. doi:10.1111/bju.12860. Epub 2014 Dec 7. PMID: 25041087.

* * * *

Brief explanation of the Exhibits

1. In **Exhibit 19** Dr Popert reacts to the statements made by Prof Debruyne.

2. He begins by noting that:

> "*Prof. Debruyne does not suggest that anything resembling the PrecisionPoint device had been disclosed prior to April 2014".*
>
> and
>
> *"[n]or does he state anywhere in his opinion that he thinks such a device would have been obvious to a skilled urologist in 2014*".

3. Dr. Popert further states that:

> "*It is clear that it has proved straightforward to adapt prior art devices so that they look like the PrecisionPoint™, and possess similar characteristics or advantages. I do not beleive, however, that this makes the patented PrecisionPoint ™device obvious over what went before."*

4. He then goes on to discuss Prof. Debruyne's attempt to create confusion about the use of the word "*freehand"* in the patent.

5. Dr Popert also makes it clear that and why his own experience is not limited to the UK, as Prof Debruyne wrongly suggests. He also discusses the Galfano article and the "fan" technique referred to by Prof. Debruyne. Dr Popert explains in detail why the devices and techniques in use at the priority date were different from and inferior to the invention.

6. In **Exhibit 20** Mr. Rashid also reacts to the Opinion of Prof. Debruyne. He discusses his contacts with Drs. Jos Immerzeel, a close colleague of Prof. Debruyne at his private clinic. Email correspondence from 2018 and 2019 between Mr. Rashid and Drs. Immerzeel shows that in 2018, Drs. Immerzeel was very impressed with the capabilities of the PrecisionPoint™ compared to other, known available biopsy procedures. Drs. Immerzeel was trained in the PrecisionPoint ™ technique by Dr. Popert in 2018. In May 2018, Drs. Immerzeel wrote that:

"*The PP technique is in my opinion the best method for reliable and safe diagnosis if there is no accessibility to a high quality MRI for precision-fusion techniques and should be used by the general urologists replacing the 'transfaecal' (®Popert) method*" [1].

7. Dr. Immerzeel himself became a *proctor* and trainer for other Dutch urologists interested in using the PrecisionPoint™ device.

8. In his statement, Mr. Rashid expresses his considerable surprise that the positive experiences of his close colleague with the PrecisionPoint™ device are not discussed at all in Prof. Debruyne's Opinion.

9. In **Exhibt 21** the inventor, Dr. Matt Allaway, also responds to the Opinion of Prof. Debruyne.

10. **Exhibit 22** concerns an attempt by Corbin to obtain a copy of the IFU and CE documentation in respect of the AMD SureFire Guide from AMD's European professional representative for regulatory purposes, MDSS GmbH. (Parties from outside the EU wishing to market a CE-marked product must have a European Representative. For LeapMed this was (and is) LeapMed France. For AMD, this is MDSS GmbH).

11. Ultimately, MDSS GmbH provided, inter alia, an IFU showing that AMD explicitly instructs end users of its needle guide to use the *needle guide* together with an *Introducer* or "*SFIN*" (a *SureFire Introducer Needle*, or *access needle* within the meaning of the patent). See **Exhibit 22B**, p. 7.

12. This shows that also AMD is offering for sale and selling its needle guide with the intention that third parties will use the device with an access needle to put into effect the patented invention. In other words, it is not only the additional instructions of Pelvitec B.V. (see **production 7**, Exhibits 2 and 3) that urge third parties to use the invention, but now also the official instructions of AMD itself. This constitutes indirect infringement by AMD and is also tortious towards Corbin.

13. **Exhibit 22C** relates to an unsuccessful attempt to obtain earlier versions of AMD's IFU through MDSS GmbH.

14. **Exhibit 23** is an email sent Friday (!) by Philippina Rose on behalf of Pelvitec B.V. approaches a potential customer[2] with an offer for sale realting to the LeapMed SureFire device. The name of LeapMed France SAS is mentioned as European representative for the product. The allegation in

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[1] See **production 20**, Exhibit SR-11.

[2] At least, that is what she thought. The email address to which she sent her request and the flyer was an email address used by Mr Wilco van der Lugt of BXTA in his earlier correspondence with Pelvitec.

the statement of defence that LeapMed France is not involved in marketing the device is utterly implausible in this light.

15. The same applies to the assertion in par. 67 of the statement of defence that the promotional material and IFU submitted by Corbin, originating from Pelvitec, is outdated. Here we have Pelvitec B.V., just a few weeks before the hearing in preliminary relief proceedings (!), using exactly the same promotional material to offer and sell LeapMed needle guides to potential Dutch customers.

16. **Exhibit 24** is an article by Dundee et al. from a few months after the priority date. The article discusses the disadvantages of the well-known freehand and grid- or template-based transperineal biopsy techniques.

17. The authors state that "*Our experience with FTPB [freehand transperineal biopsies] is limited and we would acknowledge it is a difficult technique to acquire*. [3]"

18. After then looking at the advantages and disadvantages of *freehand transperineal prostate biopsies* (FTPB) [4]and *template transperineal prostate biopsies* (TTPB) [5], the authors conclude on p. 682 that:

> "'*Cognitive fusion*'[6] *FTPB [freehand transperineal prostate biopsies] may be possible, but would certainly require experience* ***and probably the development of more effective 'freehand' needle guides***.
>
> *Using a combination of both FTPB and TTPB [template transperineal prostate biopsies] would seem to strike the right balance between minimising the risk of sepsis, ensuring adequate cancer diagnosis and effective use of precious resources, but we need more data on the FTPB technique. This will only come when larger institutions explore this technique and publish their experience. It may not be time yet to phase out TRB [transrectal biopsies] altogether, but we should be proactive in searching for durable and effective solutions to the sepsis challenge that blunts our advocacy of PSA screening*."

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[3] See p. 681, right column.

[4] Like the "fan" technique Prof. Debruyne refers to.

[5] These are the techniques in which a grid or template is used to make multiple perforations in the perineum.

[6] Cognitive fusion: a technique in which a previously made MRI-scan of the prostate is used to ultrasound the prostate. This is done without fusing the MRI and ultrasound images, but with the MRI images next to it. The urologist keeps the MRI images in mind while ultrasound-guided prostate biopsies are performed. An explanation of the ways in which MRI could be used, one year after the priority date, to take more focused biopsies (and/or rule out the need for a biopsy) can be found here: https://prostaatkankerstichting.nl/wp-content/uploads/2017/01/Onderzoek_naar_gerichte_biopten_van_de_prostaat.pdf

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[Underlining and boldface added].

19. The article shows that existing freehand techniques were difficult to learn and apply; and that there was a need among urologists for new and more effective freehand needles that could be used to take *freehand* transperineal biopsies. With the advent of the patent (and the PrecisionPoint device), that desire was fulfilled.

Waarvan akte!

[Signed]

Lawyer

District Court of The Hague
Corbin v Pelvitec & Another

EXPERT REPORT OF
DR. RICK POPERT MS FRCS (UROL)

I, **Dr. Rick Popert**, declare as follows:

My relevant qualifications

1. I am a Senior Consultant Urologist at Guys and St. Thomas Hospital in London. My particular specialization is in the detection and treatment of prostate cancer.

2. I received my qualifications as a medical practitioner from St. Bartholomew's Hospital Medical College, University of London, in 1985. I became a Fellow of the Royal College of Surgeons (FRCS) in 1989 and began my specialist training in Urology. During my training I carried out a period of research and was examined for Master of Surgery (MS). I completed my specialist urological training in 1996 following success in the FRCS (Urol) examination.

3. In 1996 I was appointed as a Consultant Urologist at Guys and St. Thomas Hospital in London, where I established a specialist prostate cancer service with an Oncologist.

4. Over the last 25 years this specialist prostate service has developed into one of the most comprehensive services within the UK. The prostate clinic is a multidisciplinary clinic with six consultant urologists, four radiation oncologists, two robotic fellows, a research fellow and six advanced nurse practitioners.

5. My main surgical expertise is in radical prostatectomy, prostate brachytherapy and Holmium Laser prostatectomy. Over the years my department has migrated from conventional open radical prostatectomy to a robot-assisted approach which started in 2005. Between 1996 & 2006, I did over 350 open radical prostatectomies. Since 2006, I have carried out over 800 robotic prostatectomies and have an experience of over 1100 radical prostatectomies.

6. I have probably the most experience of any UK urologist in single-visit dynamic intra-operative prostate brachytherapy, a surgical technique which is particularly well suited to those with larger prostates or who have had previous transurethral surgery. The procedure is a good alternative to radical surgery. It provides comparable disease control rates to radical surgery in patients with low-risk cancer. I have carried out more than 800 of these procedures with Dr Beaney and Dr Morris, both Consultant Oncologists.

7. For the treatment of benign prostatic disease (BPH), I introduced a Holmium Laser Prostatectomy (HoLEP) service at Guy's and London Bridge hospitals in 2002. This surgical procedure makes use of lasers and is associated with reduced bleeding and length of stay in patients with prostate volumes larger than 70 cc, compared with standard trans-urethral prostatectomy (TURP). I have carried out over 1200 holmium laser enucleations and receive tertiary referrals of patients with prostates considered too large for conventional surgery.

8. Importantly for the present proceedings, I have developed an expertise in the improvement of diagnostic biopsies in order to optimise treatment plans for patients with prostate cancer. Since 2006, I have developed improved transperineal biopsy approaches with enhanced prostate cancer localisation, as compared with the more traditional non-systematic transrectal biopsies or transperineal grid-based mapping biopsies. (I explain what each of these procedures entail in a subsequent section of this report).

9. In 2016, I was introduced by Dr. Matthew Allaway to the PrecisionPoint™ Transperineal Access System. From the latter half of 2016 to 2018 I carried out a pilot evaluation of transperineal biopsies under local anaesthesia using this device in over 160 cases. This preliminary experience was the first European report of the PrecisionPoint™ Transperineal Access System published in a peer-reviewed journal[1].

10. This publication confirmed the significant benefits associated with the new PrecisionPoint™ Transperineal Access System compared to existing transperineal and transrectal prostate biopsy procedures. Specifically, I was able to carry out MRI targeted and a full 24 – 38 core systematic transperineal biopsy which gave results comparable to our Institution Standard of the multiple perineal puncture Ginsburg Protocol using a brachytherapy grid and ultrasound probe fixed within a brachytherapy stepping unit under general anaesthesia. (Again: I explain more about the traditional transperineal biopsies below).

11. The ease with which the new biopsy procedure could be carried out under local anaesthetic was apparent from the outset. We recognised immediately that the universal adoption of the PrecisionPoint™ Transperineal Access System, combined with the new office or outpatient procedure it made feasible, would have enormous benefits for the patient.

[1] Kum F, Elhage O, Maliyil J, et al. Initial outcomes of local anaesthetic freehand transperineal biopsies in the outpatient setting. BJU Int 2018; 125: 244–52 (**Exhibit RP-1**).

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12. Specifically, it would avoid the need for general anaesthesia and reduce the morbidity associated with multiple puncture transperineal biopsies, which had to be carried out under general anaesthetic, with reported retention rates of up to 23.7%[2]. In addition, and most importantly, it would provide the opportunity to replace office based local anaesthetic Transrectal Prostate Biopsy with a safer alternative, local anaesthetic office based transperineal prostate biopsy, reducing the risk of prostate biopsy related sepsis and the need for antibiotics.

13. These predictions proved accurate. Significant departmental savings were also achieved by reducing operating costs and freeing up general anaesthesia operating lists for other procedures.

14. I was appointed as an NHS Clinical Entrepreneur in August 2018. I applied to become a fellow on the NHS Innovation Accelerator Programme (NIA) and was appointed in March 2019. The NIA is an initiative of National Health Service England which is aimed at accelerating the uptake of promising innovations for patient, population and NHS staff benefit. The PrecisionPoint™ Transperineal Access System is just such an innovation.

15. As an NIA Fellow, my goal was to scale the introduction of local anaesthetic transperineal biopsies nationally as an alternative to conventional transperineal biopsies (which were carried out under general anaesthetic) and transrectal biopsies (which were carried out under local anaesthetic, but were associated with an unacceptably high infection risk).

16. In October 2019 I decided to devote more time to the teaching and training of the techniques for local anaesthesia transperineal biopsies to urology consultants, junior doctors, urology nurses, radiologists and radiographers. I retired from full-time employment with the NHS and returned on a part-time contractual basis in order to be able to devote more time to spreading the word about local anaesthesia transperineal biopsies using the PrecisionPoint™.

17. I am a director of a company called PPDT Ltd, which has a consultancy agreement with BXTAccelyon, the UK appointed distributor of the PrecisionPoint™ device. The agreement provides for the payment of honoraria for running training courses on transperineal biopsies under local anaesthesia on top of my NHS commitments.

18. My work in training fellow urology specialists in the new local anaesthesia transperineal technique has been effective. Presently, at least 50% of all prostate biopsies in the U.K. are carried out using the new local anaesthetic transperineal techniques first made possible by the PrecisionPoint™ system.

19. I attach a copy of my curriculum vitae together with a list of publications as **Exhibit RP-2.**

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[2] Retention refers to difficulties experienced by patients passing water. The figure of 23.7% comes from Simmons, L., Kanthabalan, A., Arya, M. et al. *The PICTURE study: diagnostic accuracy of multiparametric MRI in men requiring a repeat prostate biopsy.* Br J Cancer 116, 1159–1165 (2017). https://doi.org/10.1038/bjc.2017.57

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My instructions

20. I have been asked by Dutch counsel acting for Corbin Clinical Resource LLC. ("Corbin") to explain how conventional prostate biopsies were carried out, and to say something of the impact PrecisionPoint™ device has influenced how urologists conduct such biopsies now.

21. I understand that this report will be referred to by Corbin in Dutch proceedings against Leapmed and its Dutch distributor Pelvitec. It has been explained to me, and I understand, that it is my duty honestly to assist the Dutch Court with matters falling within my area of expertise, and that this duty outweighs any duty I may feel I owe to those instructing me. The facts stated in this report are true to the best of my knowledge and belief and the opinions stated herein are truly held.

22. It has been explained to me, and I believe, that the PrecisionPoint™ device is a commercial embodiment of the devices claimed in European patent EP 3 125 811 B1. I have studied the claims, description and drawings of EP 3 125 811 B1 and have satisfied myself that the PrecisionPoint™ indeed corresponds to the devices set out in the claims and in the schematic drawings of the patent.

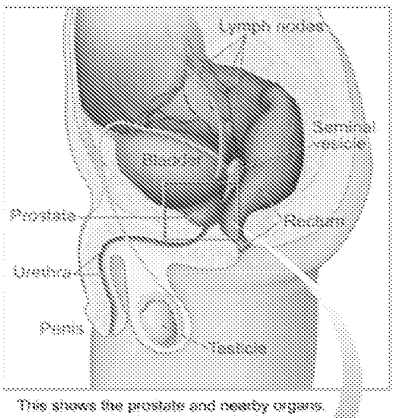
23. It has been explained to me that the priority date of EP 3 125 811 is 3 April 2014, and that it is this date, and not the later date of introduction of PrecisionPoint™ device (or the date of my first experiences with the device), which is important when it comes to discussing conventional biopsy procedures. I confirm that when I discuss conventional prostate biopsy techniques in what follows, I have endeavoured to do so, to the best of my ability, from the point of view of a skilled urologist as of early 2014.

Prostate cancer and biopsies

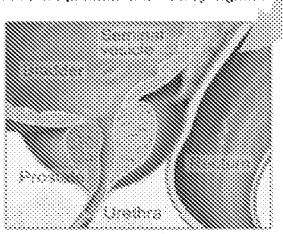
24. The prostate is a gland that is part of the male reproductive system. Anatomically, it is situated below the bladder, with the urethra passing through it.

25. The prostate has two functions. The first is that it produces and contains fluid that forms part of the semen that is emitted during ejaculation. The second function of the prostate is that it functions as a muscle-driven mechanical switch between urination and ejaculation. During ejaculation, muscles in the prostate close the urethra up to the bladder to prevent semen from entering the bladder.

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This shows the prostate and nearby organs.



This shows the inside of the prostate, urethra, rectum, and bladder.

26. In Europe, prostate cancer is the most common form of cancer occurring in men. In the UK, approximately 1 in 8 men will suffer prostate cancer at some point in their lives. It is more prevalent in men over the age of 50. Across the UK, more than 47,500 men are diagnosed with prostate cancer every year.[3]

27. In The Netherlands, I have been informed, and I believe, that the latest available statistics show that 12,800 cases of prostate cancer were diagnosed in 2020, down from 13,478 in 2019. The decreased incidence in 2020 is believed to be due to the COVID-19 pandemic and the associated restrictions on hospital visits and visits to the doctor, where prostate problems often emerge as a result of opportunistic screening using a PSA test when the patient is visiting his GP for other reasons.[4]

28. The first step to a diagnosis of prostate cancer usually involves a blood test that screens for Prostate Specific Antigen (PSA). This is a protein produced by both healthy and unhealthy prostate cells. Elevated PSA levels can be indicative of prostate cancer. A doctor may also perform a digital rectal examination to feel the back wall of the prostate for enlargement, tenderness, lumps or other abnormalities.

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[3] https://prostatecanceruk.org/prostate-information/about-prostate-cancer.

[4] https://www.volksgezondheidenzorg.info/onderwerp/prostaatkanker/cijfers-context/huidige-situatie#node-het-v%C3%B3%C3%B3rkomen-van-prostaatkanker

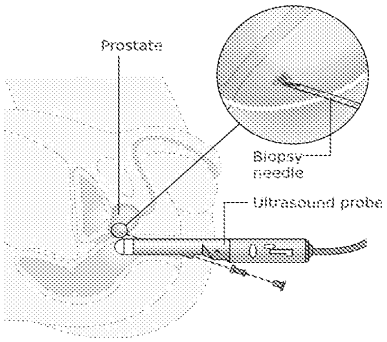
29. If either of these tests indicate a risk of prostate cancer, a biopsy will be required to collect tissue samples for pathological analysis. This is the only reliable way to establish whether a patient indeed has prostate cancer.

30. Roughly 50% of all patients who undergo a prostate biopsy will test positive for cancer.

The previous gold standard of care: transrectal ultrasound biopsies (TRUS)

31. Until a few years ago, the standard of care for performing a prostate biopsy was the transrectal approach guided by an ultrasound probe, abbreviated to TRUS (for TRansrectal UltraSound).

32. This technique, which had been the gold standard for well over 30 years, was first reported in 1981 by Holm et al.[5] In this procedure, the prostate is accessed via the rectal wall. The biopsy needle is advanced along a needle guide through the rectal passage and pierces the rectum to reach the prostate. An ultrasound probe is used to determine and guide the position of the biopsy needle.



33. In a TRUS procedure, tissue samples are taken from a number of different areas of the prostate (typically 6 to 12 different cores), which are then sent to the pathology laboratory for analysis.

34. A benefit of the transrectal approach is that it can be carried out under local anaesthetic. It does not require a visit to an operating theatre and can instead be carried out in an out-patient (or office) setting. Patients can go home the same day, following a short post-intervention monitoring period. The procedure can be carried out by Urologists, Urological Trainees, Urology Specialist Nurses, Radiologists and Radiographers

35. There are however also serious drawbacks associated with this technique.

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[5] Holm et al, *Ultrasonically guided precision needle placement in the prostate and seminal vesicles*, J Urol 1981; 125:385-387.

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36. First, not all regions of the prostate are easy to access via the transrectal route, particularly the anterior prostate. This can lead to tumours going undetected, and disease being mischaracterised[6].

37. Second, TRUS is, by its nature, a non-sterile procedure. The biopsy needle must pass first through the rectal cavity before entering the prostate. The introduction of faecal matter by the repeated passage of the contaminated biopsy needle into the prostate poses a significant infection risk. Steps can be taken to minimize the risk, but local inflammation, pain, shivers and fever are commonly reported following a TRUS biopsy.

38. There is also a risk of post-biopsy related sepsis, a very serious life-threatening infection, which can result in life-changing disability and even death. A publication by the European Association of Urologists puts the risk of sepsis in a standard TRUS procedure as high as 2.2%.[7] Bearing in mind that half of all patients undergoing a biopsy procedure will test negative for cancer, such an adverse risk percentage is significant for a benign condition.

39. Due to the "contaminated" nature of the TRUS biopsy procedure, patients are commonly prescribed antibiotics both before and after the procedure. Antibiotics have never been 100% effective at preventing the infection risks associated with the procedure, but in recent years the increased prevalence of antibiotic resistance and the emergence of multi-resistant bacteria in rectal flora has become a real problem. Increasing antibiotic resistance has led to the incidence of adverse effects and sepsis following a TRUS biopsy increasing over recent years. Moreover, the European Union has recently banned the prophylactic use of fluoroquinolones which were the gold standard prophylactic in use for transrectal biopsies.[8]

Transperineal biopsy

40. As an alternative to the transrectal route, the prostate can be accessed via the perineum. The perineum is the area of skin between the scrotum and the anus. A schematic illustration is reproduced below, showing how the biopsy needle punctures the skin of the perineum and passes through the tissue behind it to arrive at the prostate.

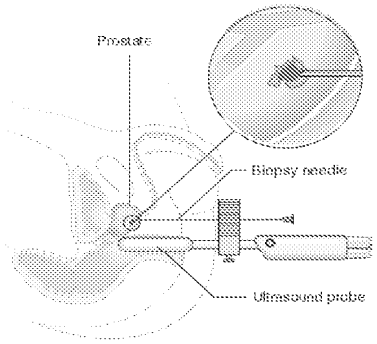
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6 Evans et al., "The Use of Transperineal Sector Biopsy as A First-Line Biopsy Strategy: A Multi-Institutional Analysis of Clinical Outcomes and Complications", Urol J, 2016 Oct 10;13(5):2849-2855. **Exhibit RP-3**. See page 2849, left column.

7 Bonkat et al., *Time to Adapt Our Practice? The European Commission Has Restricted the Use of Fluoroquinolones since March 2019*, European Urology, Volume 76, Issue 3, Pages 273-275. See page 275 left column: *"All the studies included except for one were cohort studies and included a combination of retrospective and prospective data. The authors calculated a sepsis rate of 2.21% (95% CI 1.71–2.87%) in the standard prophylaxis group compared to 0.48% (95% CI 0.26–0.88%) in the targeted prophylaxis group (p < 0.001)."*

8 See: Pilatz A, et al. *European Association of Urology Position Paper on the Prevention of Infectious Complications Following Prostate Biopsy*. Eur Urol (2020), https://doi.org/10.1016/j.eururo.2020.10.019, at page 2.

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41. An advantage of the conventional transperineal technique over the transrectal technique is that the biopsy needle is not required to pass through the non-sterile tissues of the rectum. There is therefore no risk of introducing faecal matter into the prostate. The risks and incidence of infections is much lower with a transperineal procedure.

42. Another advantage of the transperineal approach is that the different orientation allows access to parts of the prostate (in particular the anterior prostate) that are difficult to reach via the transrectal route.

43. The major disadvantage was that the need to make multiple perineal punctures during a template-mapping transperineal biopsy required a general anaesthetic, because of patient discomfort. For each sample taken, the biopsy needle had to be repositioned and a new puncture path through the perineum and intermediate tissue into the prostate had to be made. The original description of transperineal mapping biopsy required one core to be taken for every cubic centimetre of the prostate. A standard prostate volume of 30cc would require 30 cores, 50cc up to 50 cores, and 100cc up to 100 biopsy cores.[9] Each core taken required a separate puncture of the skin and perineal tissue.

44. To aid the urologist to systematically carry out the multiple perineal puncture biopsies, the standard procedure was to use a brachytherapy grid template to guide the biopsy needle. I have reproduced an example below, showing a grid of 13 x12 positions (making for 156 potential distinct puncture holes). The combination of grid and probe is attached in a fixed position on to a stepper unit which allows the fixed probe to be advanced into the patient's rectum to visualize the prostate by ultrasound and to position the grid against the patient's perineum. The whole system is supported by a stabilization arm which is fixed to the operating table. The system is complicated to set up, is heavy and cumbersome, and requires cleaning after every procedure. It also requires specialist training to be used properly.

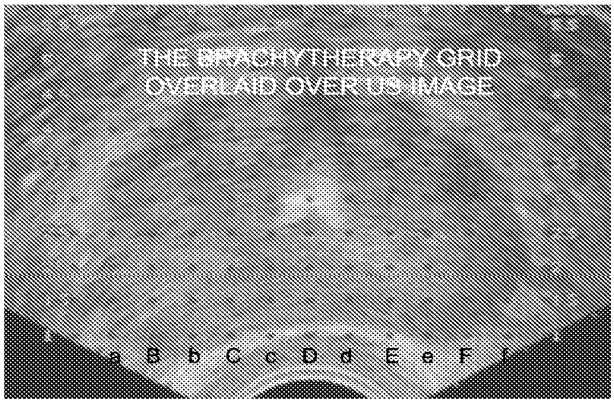
[9] See Evans et al. (**Exhibit RP-3**), page 2852 table 7.

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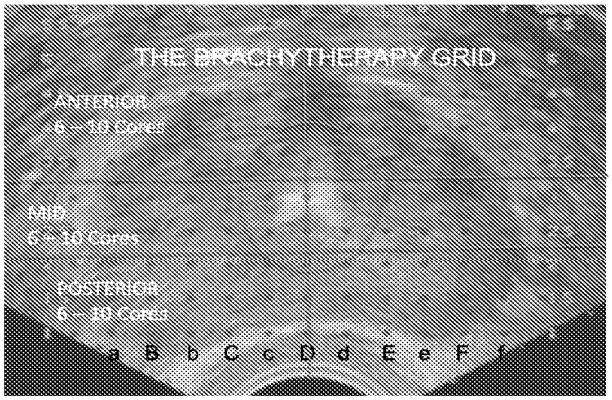
Brachytherapy grid, ultrasound probe fixed to stepping unit and stabilisation arm with sterile drape

45. Once the ultrasound probe has been advanced into the rectum the prostate is visualized. The brachytherapy grid is advanced so that it rests against the perineum. An image of the brachytherapy grid is overlaid on the ultrasound screen by the ultrasound software. The surgeon uses the apertures of the grid as a needle guide, to insert the biopsy needle through the grid apertures which overlay the prostate image, through the superficial perineal skin, the deep perineum and finally into the prostate to sample different areas of the prostate gland, avoiding, if possible, the central area containing the urethra.

46. The images below show that for a normal sized prostate of 30 – 40 cc, it is necessary to take between 36 – 60 samples through multiple separate punctures.



An average sized prostate of 30 - 40 cc



36 – 60 Cores (separate punctures) taken in an average sized prostate

The central urethral area is outlined in red

47. It will be appreciated that this transperineal procedure, while "cleaner" than the transrectal procedure, was much more invasive, and associated with much more discomfort to the patient, compared to the transrectal route, such that it almost invariably had to be carried out under a general anaesthetic.

48. The equipment in common use for perineal biopsies at the priority date, and the requirement for general anaesthesia, made this a resource-intensive and costly procedure. To conduct a perineal biopsy, an operating theatre, a specialist trained urologist and associated specialist staff, including an anaesthesiologist, would be required.

49. As compared to transrectal biopsy, significantly more hospital time is required per patient with a transperineal approach under general anaesthetic, both during the procedure, as well as post-procedure. Transperineal grid biopsy under general anaesthetic generates waiting lists and leads to delays in diagnosis (and ultimately treatment). Although it is associated with less sepsis than TRUS biopsy, it is recognised that there is a greater risk of other complications, including bleeding, worsening urinary symptoms and retention of urine, which can also result in urinary sepsis.

50. In summary, although transrectal biopsies are simple to perform under local anaesthetic in the outpatient environment, they are associated with an unacceptable risk of sepsis. Transperineal mapping biopsies provide a more comprehensive biopsy but require complex equipment and a general anaesthetic. The morbidity associated with this procedure is associated with other complications such as retention of urine and urinary sepsis.

51. Prior to the arrival of the PrecisionPoint™ device, we did attempt to carry out transperineal biopsies using local anaesthetic as an alternative to LA TRUS. Our work on local anaesthetic grid-based transperineal biopsies was completed in 2009 and published in 2014[10].

52. We completed a pilot of 50 cases which confirmed that a local anaesthetic transperineal procedure could be carried out in the outpatient setting. The procedure was considered tolerable but I would not describe it as comfortable. We were unable to incorporate this approach in our routine practice: it was too complex, labour-intensive and time-inefficient for the outpatient environment. We continued to do TRUS biopsies under local anaesthetic in the outpatient setting and transperineal biopsies unde general anaesthetic in selected patients. It was not until 2016, when I was introduced to the PrecisionPoint™ Transperineal Access System, that a viable alternative became available.

The PrecisionPoint™ device

53. Prior to the patent (again, in fact prior to the advent of the PrecisionPoint™ transperineal access system), urologists were thus effectively faced with a choice between transperineal biopsies under general anaesthesia or transrectal biopsies under local anaesthesia.

54. As will be appreciated from what is set out above, transrectal biopsies had the benefit of being quick and cost-effective, and could be carried in the out-patient setting under local anaesthetic, but they came with a significant and increasingly unacceptable risk of infections and potential missed diagnoses. Transperineal biopsies, on the other hand, had a lower risk of infection, but were more complex to carry out and required general anaesthesia (which in turn meant they had to be carried out in operating theatres).

55. In general, clinicians adopted a policy according to which patients were stratified by risk to one or the other. A policy adopted across our cancer network was that all patients who had a previous negative transrectal biopsy would be offered a transperineal biopsy. All patients being considered for active surveillance were offered a confirmatory transperineal biopsy. Patients at risk of sepsis, diabetics, and the immune-compromised were recommended to have a transperineal biopsy, rather than a TRUS biopsy.

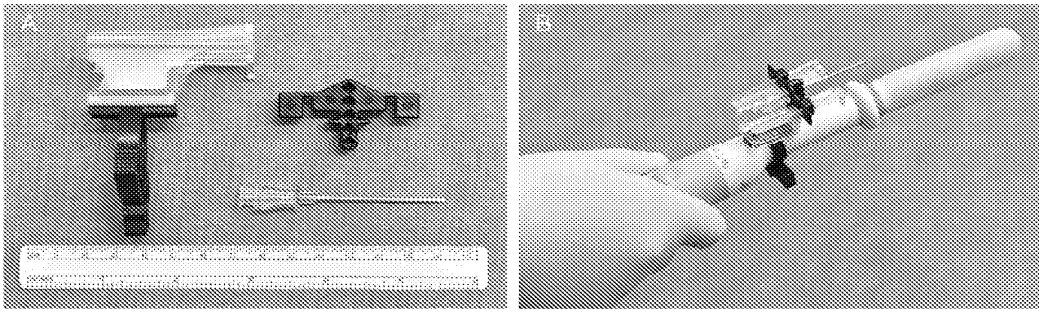
56. In 2016, I was introduced to the PrecisionPoint™ Transperineal Access System, a device that resolves the dilemma facing clinicians. With the PrecisionPoint™ device, it is possible to perform both targeted and systematic transperineal prostate biopsies under local anaesthetic, in an outpatient setting, using only two perineal puncture sites. The device has an innovative design that makes it simple to use, efficient and significantly cheaper than the traditional transperineal equipment. It can be used in conjunction with commonly available handheld rectal transducer probes.

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[10] Smith JB, Popert R, Nuttall MC, Vyas L, Kinsella J, Cahill D, *Transperineal sector prostate biopsies: a local anesthetic outpatient technique*, Urology 2014 Jun;83(6):1344-9 (**Exhibit RP-4**).

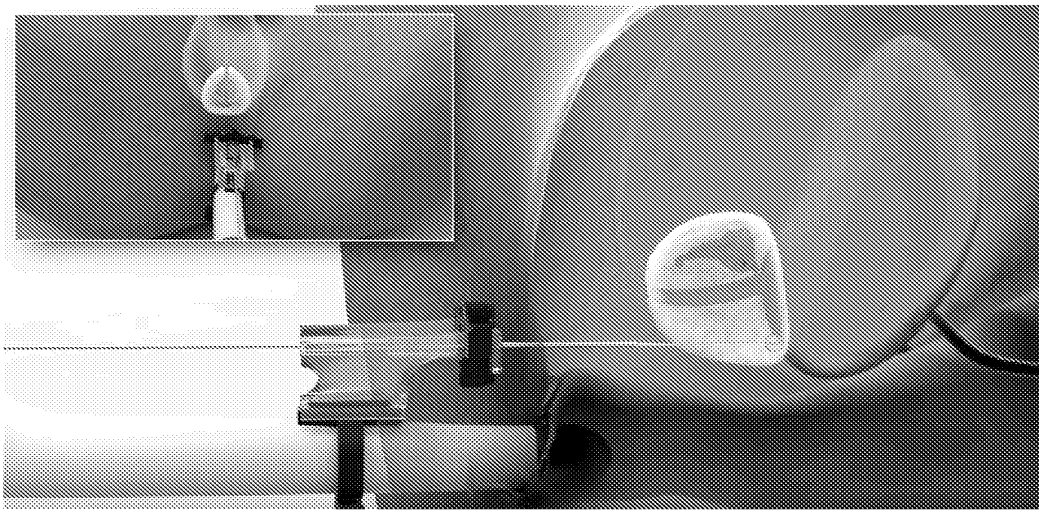
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57. I have reproduced an image of the PrecisionPoint™ system, including how it attaches to a held hand transducer, below.



58. A unique feature of the PrecisionPoint™ device is that it uses an access needle intended for the introduction of the biopsy needle. This access needle is the needle shown above.

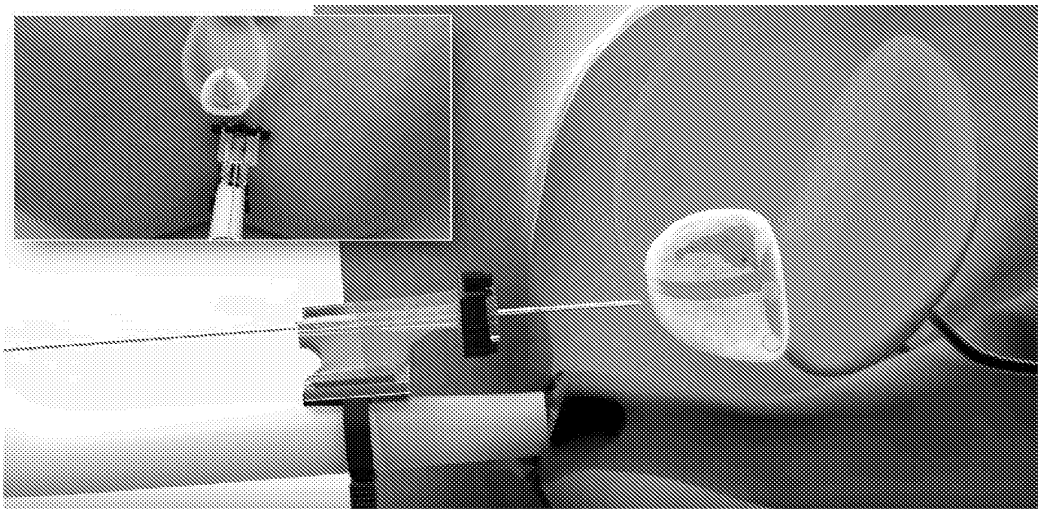
59. The access needle is used first to guide the local anaesthetic infiltration of the skin and periprostatic tissues. Once anaesthesia has been confirmed, prostate biopsies are taken by advancing the biopsy gun needle through the access needle. Multiple subsequent biopsy cores can then be taken, via the access needle, *through the same hole in the perineum*. By tilting or angulating the access needle which is linked to the probe with the attached PrecisionPoint™ device, the clinician can target different sites of the prostate through one and the same perineal puncture point. An explanatory animation video is available on YouTube[11], and I have reproduced two screenshots from the video below.



[11] https://www.youtube.com/watch?v=vV60sUQexuE

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60. The ability to take multiple biopsy samples through a single access hole has made it possible to carry out perineal biopsies under local anaesthetic in the outpatient setting. Using the PrecisionPoint™ device, it is possible to sample the entire prostate through just two punctures in the perineum: one to the left of the urethra, and one to the right.

61. The procedure is extremely well tolerated by patients and takes a comparable amount of time as a transrectal biopsy. Importantly, it has proved straightforward to teach urologists, specialist urology nurses, radiologists and radiographers how to use the device effectively. The introduction of the PrecisionPoint™ Transperineal Access System has revolutionised prostate biopsy procedures within the UK by removing the major barrier that prevented transperineal biopsies from being carried out on a larger scale.

Perineal biopsies are now well on the way to completely replacing TRUS biopsies in the UK

62. In the UK, thanks to our success at Guy's Hospital, and to the willingness of fellow consultant urologists to embrace the opportunity to transform prostate biopsy practice, within six months of CE approval, there were 12 urology centres routinely using the device. By December 2019, this had grown to over 70 centres. As of the end of June 2021, 141 centres use the device routinely.

63. The COVID-19 pandemic has, if anything, accelerated the adoption of the PrecisionPoint™ device. Transperineal biopsies have, as I explain above, the advantage that they have a much lower risk of infection and hospitalization post-procedure. That is key in a setting where hospital capacity was already stretched beyond its limits. The unique quality of the PrecisionPoint™ procedure is that it can be carried out under local anaesthetic, in the outpatient setting, freeing up valuable anaesthetic resources for other procedures.

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64. Our experience of TP biopsies during the pandemic was published in 2020[12] and indicated that during the pandemic that there was increased adoption of LA TP biopsies, with less GA TP biopsies and reduced use of TRUS Biopsies compared to before the advent of the pandemic.

65. NHS Hospital Episode Statistics show that between 2007 – 2011 transperineal biopsies accounted for 23,000 of 183,000 prostate biopsies (12.5% of all biopsies). Between 2012 & 2017, this had increased to 25% of all biopsies. From 2018 (the introduction of the PrecisionPoint™ in the UK following CE Mark), this had grown to 42% of all biopsies by April 2020 (pre-pandemic). Since the pandemic, transperineal biopsies now account for 65% of all prostate biopsies (April 2021 data).

66. This transformational change of practice has been termed the TREXIT Initiative. This transformation of biopsy practice is directly related to the introduction of the PrecisionPoint™ Access System.

The PrecisionPoint™ in the scientific literature

67. The arrival of the PrecisionPoint™ has been welcomed in the scientific press. Thus, in Kum F et al, *Initial outcomes of local anaesthetic freehand transperineal prostate biopsies in the outpatient setting*. BJU Int. 2020 Feb;125(2):244-252. doi: 10.1111/bju.14620. Epub 2019 Dec 3. PMID: 30431694 (**Exhibit RP-5**), the authors[13] looked at results from 176 patients and concluded that:

> "*Freehand transperineal biopsies using the PrecisionPoint™ access system is a safe, tolerable and effective method for systematic and targeted biopsies under local anasthaesia in the outpatient setting. It has replaced transrectal biopsies in our centre and has potential to transform practice*".

68. In another article, Lopez JF et al, *Local anaesthetic transperineal (LATP) prostate biopsy using a probe-mounted transperineal access system: a multicentre prospective outcome analysis*. BJU Int. 2021 Sep;128(3):311-318. doi: 10.1111/bju.15337. Epub 2021 Apr 12. PMID: 33448607 (**Exhibit RP-6**), the authors[14] looked at a much larger cohort of patents (1218 in all) from a number of different treatment centres and concluded that the data suggested that:

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[12] Stroman L, Cathcart P, Lamb A, Challacombe B, Popert R, *A cross-section of UK prostate cancer diagnostics during the coronavirus disease 2019 (COVID-19) era - a shifting paradigm?* BJU Int. 2021 Jan;127(1):30-34.

[13] I am one of the authors of this article. The full list of authors comprises colleagues from Kings College School of Medicine and from Guys: Kum F, Elhage O, Maliyil J, Wong K, Faure Walker N, Kulkarni M, Namdarian B, Challacombe B, Cathcart P, and Popert R.

[14] Again, I was one of the authors of this article. The full list of authors is as follows: Lopez JF, Campbell A, Omer A, Stroman L, Bondad J, Austin T, Reeves T, Phelan C, Leiblich A, Philippou Y, Lovegrove CE, Ranasinha N, Bryant RJ, Leslie T, Hamdy FC, Brewster S, Bell CR, Popert R, Hodgson D, Elsaghir M, Eddy B, Bolomytis S, Persad R, Reddy UD, Foley C, van Rij S, Lam W, and Lamb AD.

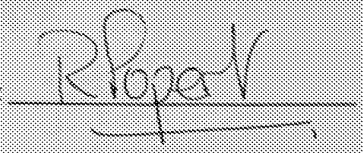
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"[local anaesthaesia transperineal biopsy] using a TP access system is feasible, mounted to the ultrasound probe achieves excellent PCa detection, with a very low sepsis rate, and is safe and well tolerated."

69. They noted that a randomised controlled trial comparing local anaesthesia transperineal biopsies with transrectal ultrasound-guided biopsies (TRUS) to investigate the relative trade-offs between each biopsy technique would be helpful.

Statement of truth

70. The facts stated in this report are true to the best of my knowledge and belief and the opinions stated herein are truly held. What is set out above is based on my own knowledge and experience, and represents my complete and professional opinion. I am prepared to attend Court and confirm the contents of this expert report under oath.

Signed: 

Dr. R. Popert

On this day of October 2021

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List of Exhibits

RP-1 Kum F, Elhage O, Maliyil J, et al. *Initial outcomes of local anaesthetic freehand transperineal biopsies in the outpatient setting,* BJU Int 2018; 125: 244–52

RP-2 Curriculum vitae and list of publications

RP-3 Evans et al., *The Use of Transperineal Sector Biopsy as A First-Line Biopsy Strategy: A Multi-Institutional Analysis of Clinical Outcomes and Complications* Urol J, 2016 Oct 10;13(5):2849-2855

RP-4 Smith JB, Popert R, Nuttall MC, Vyas L, Kinsella J, Cahill D, *Transperineal sector prostate biopsies: a local anesthetic outpatient technique*, Urology 2014 Jun;83(6):1344-9

RP-5 Kum F, Elhage O, Maliyil J, Wong K, Faure Walker N, Kulkarni M, Namdarian B, Challacombe B, Cathcart P, Popert R, *Initial outcomes of local anaesthetic freehand transperineal prostate biopsies in the outpatient setting*. BJU Int. 2020 Feb;125(2):244-252. doi: 10.1111/bju.14620. Epub 2019 Dec 3. PMID: 30431694

RP-6 Lopez JF, Campbell A, Omer A, Stroman L, Bondad J, Austin T, Reeves T, Phelan C, Leiblich A, Philippou Y, Lovegrove CE, Ranasinha N, Bryant RJ, Leslie T, Hamdy FC, Brewster S, Bell CR, Popert R, Hodgson D, Elsaghir M, Eddy B, Bolomytis S, Persad R, Reddy UD, Foley C, van Rij S, Lam W, Lamb AD, *Local anaesthetic transperineal (local anasthaesia transperineal) prostate biopsy using a probe-mounted transperineal access system: a multicentre prospective outcome analysis*. BJU Int. 2021 Sep;128(3):311-318. doi: 10.1111/bju.15337. Epub 2021 Apr 12. PMID: 33448607

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BarentsKrans

135701
Court of The Hague in preliminary relief proceedings Sitting: Tuesday, 30 November 2021
Case/short title: 619229 / 21-974

INSTRUMENT ON THE PRODUCTION OF COUNTER-PRODUCTIONS

On the subject:

1. the company under foreign law
   ADVANCE MEDICAL DESIGNS INC.,
   located in Marietta, GA, United States of America,

2. the private company
   PELVITEC B.V.1,
   established in Delft,

3. LEAPMED FRANCE SAS, a
   company governed by foreign law,
   having its registered office in
   Nailloux, France,

4. Mr
   NICO EELBODE,
   with its registered office in Ostend, Belgium and its registered office in Nailloux, France,

Defendants,
Lawyers: J.J.E. Bremer and A.H. van Duijn versus:

the company under foreign law
CORBIN CLINICAL RESOURCES LLC,
located in Cumberland, MD, United States of America,
plaintiff,
lawyers: S.C. Dack and P. van Schijndel.

BarentsKrans

Defendants (hereinafter **AMD et al.)** seek notice of the following:

1 In addition to its **Productions GP01 to GP46,** AMO c.s. brought the following reactive **Productions GP47 to GP49** into dispute.

2 Below follows a summary of the reactive productions, with a short explanation of each production. An **updated production overview** is also attached to this deed.

Productio n	Brief explanation
GP47	This is a statement of urologist Assoc. Prof. Frantisek Zat'ura, M.D., Ph.D. **("Zat'ura"),** and an affidavit in Dutch, in which he responds to the concurring contentions of (inter alia) Dr. Popert **(Production EP19, inter alia** para. 5 and para. 47) and Allaway **(Production EP21, inter** alia para. 25) that a needle guide in combination with an access needle would not have been disclosed before April 2014. Zat'ura states that in the 1980s he used BK Medical's UA0650 needle guide (which is similar to the UA1232 and UA1324, among others) on a probe in conjunction with an access needle for transperineal prostate biopsy, among other things. All of this was done publicly. Furthermore, Zat'ura confirms that the manual (attached to the declaration) of the BK Medical probe type 1850 recommends the use of the UA0650 needle guide in combination with an access needle in the case of biopsy with a fine needle. This is to prevent the fine needle from "straying" from the chosen direction. Thus, Corbin's assertion is incorrect. The use of a needle guide in combination with an access needle for transperineal prostate biopsy does belong to the state of the art. Both the statement of Za'tura as well as the manual of the 1850 probe confirm this.
GP47.1	This is a publication in honor of Zat'ura's *1oe* birthday, and a certified Dutch translation of this publication, with information about his long career in urology and mention of his experience with transoerineal orostatic biosis in the 1980s.
GP47.2	This is the user manual for Tru-Cut® Soft Biopsy Needles. It follows that biopsy needles can also include an access needle. EP811 in no way implies that the use of these biopsy needles is not covered by the term 'access needle' as used in the conclusions of EP811. It follows from **Production GP33** (submitted to the CoA) that Tru Cut® Soft Biopsy Needles were already generally available on the market for use in biostat biopsies in 2011.

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GP47.3	This concerns the user manual from 2006 of the endosonic probe type 1850 by BK Medical. Even earlier versions of this manual exist, but could not be found within the short time frame of these preliminary relief proceedings. In any case, the manual dates from before April 2014. See also the explanation at **Production GP47**.
GP48	This is a statement from fusion biopsy specialist Jos J. Immerzeel MD **("Immerzeel").** Immerzeel responds to the statements of Popert, Rasheed and Allaway (**Productions EP19, EP20 and EP21** respectively**).** Immerzeel explains that and why Popert and Rasheed falsely pretend that he was an *"enthusiastic advocate"* of the PrecisionPoint. His involvement saw something quite different, and that was the application of his local anesthetic technique with the PrecisionPoint. However, Immerzeel had little faith in PrecisionPoint itself, as evidenced by the fact that he was only willing to work with BXTA/PrecisionPoint for a relatively short time. Further, Immerzeel addresses comments made by Popert and Allaway regarding the BK1324 and Onik. In particular, Immerzeel explains that and why it is not new and inventive to use an access needle in a needle guide such as the BK1324. Further, Immerzeel explains that all needle guides - whether the BK needle guides, the PrecisionPoint, the SureFire, or the needle guide from Onik - are pressed against the perineum, ensuring that, as with the fan technique, when the needle is positioned, it can continue to protrude through the same opening without tearing out the perineum. The principle is the same when using a touana needle as when using an aewborn needle.
GP48.1	This is the curriculum vitae of Jos. J. Immerzeel MD, dated 2021.
GP49	This is the current brochure for the SureFire device, submitted in response to **Production EP23.** Ms Rose of Pelvitec mistakenly emailed an outdated brochure to Mr Van der Lugt (with the Leapmed logo in place of the AMO logo). That this brochure is out of date is also clear from **Production EP23,** since the brochure states in the footer on page 2 the year 2020 *"V1.0 UR 2020 03"* and *"© 2020"*. These mentions are in line with paragraphs 67-68, 251- 252 CoA, where it is explained that since the end of 2020, the supply of the SureFire in all countries worldwide except China has been provided exclusively by AMD (and therefore not by Leapmed). Going forward, Pelvitec will only use the AMO brochure, as shown in **Production GP49.** Pelvitec hereby gives its word. It goes without saying that

Leapmed cannot be held responsible for the fact that Pelvitec (incidentally) did not wrong, old brochure.

3 AMO c. s. furthermore objects to the submission of Production EP22 (including parts A, B and C) as a reactive production by Corbin. Parts A and B namely concern an e-mail including attachments of 13 October 2021, whereas a summons was issued on 21 October 2021 (more than a week later). Therefore these documents could (and should) have already been submitted with the summons. This production is not a reaction to any production submitted by AMO et al. by way of reply, whereas this is required according to section 9 of the instructions for cart proceedings that the parties received from the Court, in order to be allowed as reactive production. Part 9 states: *"Only reactive productions of the plaintiff (i.e. productions in reaction to the productions that the defendant submitted in its reply to the statement of defence)". It* is not clear from the accompanying Corbin memorandum to which production of AMO et al. Production EP22 is a reaction, nor why this production could not already have been submitted with the summons. As regards part C, this production largely consists of the e-mail string that also already appears in part A. For the same reason, part C can therefore be used as a basis for a reply. For the same reason, subsection C cannot be submitted.

4 AMO et al. also objected to the submission of Production EP23. According to the accompanying document, this production is a reaction to the reply to the action. However, it is not allowed to respond to the reply to the statement of defence, because, as mentioned above, only *"productions ! response to the productions'* are allowed. For this reason, Production EP23 must be rejected.

5 AMO et al. further objected to the submission of Production EP24. Nowhere did Corbin substantiate to which production of AMO et al. this production would be a reaction and why submission was not possible upon summons.

6 AMO c. s. request that you refuse to accept Productions EP22, EP23 and EP24 for the aforementioned reasons.

WHEREAS!

Advocaten

This case is being handled! J. J. E. Bremer and A.H. van Duijn, BarentsKrans Cooperatief U. A. , PO Box 30457, 2500 GL The Hague, telephone: 070-376 06 25, fax: +31 70 360 16 85, e-mail addresses: jaap.bremer@barentskrans.nl and allard.vanduijn@barentskrans. nl.

Comments

BJUI
BJU International

Transperineal prostate biopsy: template-guided or freehand?

Philip E. Dundee*†, Jeremy P. Grummet‡ and Declan G. Murphy*†§

*Royal Melbourne Hospital, ‡The Alfred Hospital, §Peter MacCallum Cancer Centre, University of Melbourne, Melbourne, and †Epworth Prostate Centre, Epworth Healthcare, Richmond, Vic., Australia

This Journal and others have recently hosted a number of papers that have increased interest in the use of a transperineal approach for prostate biopsy [1–3]. Much of the background to this is the gradual but steady increase in the incidence of infectious complications after TRUS-guided biopsy of the prostate (TRB) [4–7].

The increase in infections and urinary sepsis after TRB can be linked to the emergence of coliforms resistant to quinolone antibiotics. In several recent publications, the incidence of sepsis after TRB has been as high as 5% [1]. Risk factors for bacterial resistance have been well described and are related to the widespread and sometimes inappropriate use of antibiotics, particularly the quinolones.

Some infectious disease specialists consider we have already entered the post-antibiotic era and it is clear that we need a strategy to minimise further emergence of resistant bacteria, as well as reducing the current infection and sepsis rates after biopsy. Although strategies have been described to reduce the risk of sepsis after biopsy, all but transperineal biopsy (TPB) have failed to eliminate the need for quinolone prophylaxis or sufficiently reduce the rate of septic complications.

TPB has the advantage of avoiding penetration of the rectal mucosa and thus minimising inoculation of the prostate with bowel flora. The perineal skin can be prepared with antiseptic solution in a way that rectal mucosa cannot. Of the many published series of TPB experience, the incidence of sepsis is either zero, or close to zero and non-life threatening UTIs are uncommon [1,3,8]. Patients in these series are often at increased baseline risk for sepsis, having received prior quinolone antibiotics for negative TRBs. The advice from our infectious diseases colleagues is that cephazolin provides adequate coverage for a TPB procedure, dispensing with quinolone antibiotics altogether. Cephazolin provides prophylaxis against most urinary pathogens and is less resistogenic than the quinolones.

The most recent commentary, however, has evolved around template TPB (TTPB), which uses a brachytherapy stepping unit and grid, a sophisticated ultrasound and biplanar ultrasound probes. The acquisition of this equipment is expensive, but it is the requirement for general anaesthesia that poses the most significant resource issue for urologists and institutions looking to embrace the transperineal approach for one of the most commonly performed urological procedures.

But we may be overlooking a cheaper, faster and more accessible solution. TPB was originally described as a freehand TPB (FTPB) procedure, using just a standard TRUS unit and either linear, convex or biplanar probe, (although the best views are obtained with a linear array probe). It does not require general anaesthesia, vastly reducing the resources required and the time taken to perform the procedure in comparison to a TTPB. Many different techniques have been described, with both a pure freehand technique, or with a probe mounted needle guide. FTPB has been described in the lateral position, even without the need for local anaesthesia, using just a single midline puncture in the perineum. However, FTPB is most commonly described in lithotomy and is usually performed under local anaesthesia, with or without sedation. A single skin puncture in the midline just above the anus with a wide bore needle through which all cores are obtained allows access to the whole gland, but does risk puncturing the urethra, particularly when sampling the anterior part of the prostate. Alternatively, bilateral punctures can be performed to avoid the urethra (Fig. 1).

Our own experience with FTPB is limited and we would acknowledge it is a difficult technique to acquire. Passing a needle accurately without a needle guide takes skill and sampling the base of the prostate, particularly in large glands, is more difficult than with a transrectal technique. Any urologist with experience of TTPB or brachytherapy will be aware of tricks to guide the tip of the needle to a desired location, including the speed of thrust and the direction of the bevel to deflect the needle. These techniques can be both effective and frustrating in equal measure with FTPB during the learning curve. One solution is to perform both TRB and

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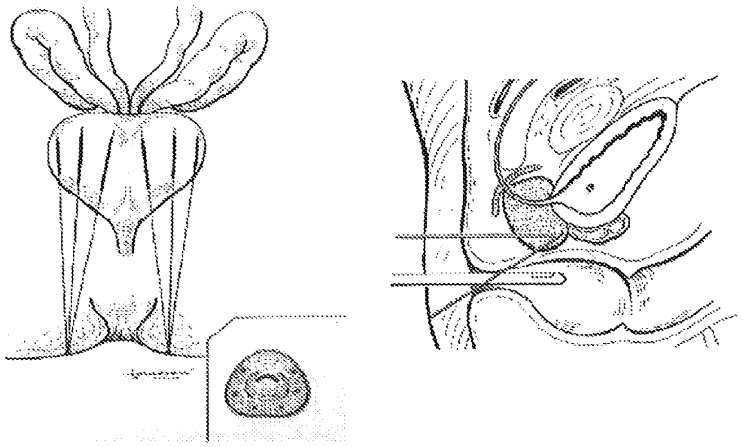


Fig. 1 Schematic for freehand transperineal biopsy [9].

FTPB until comfortable with the latter technique in order to reduce the risk of decreasing cancer detection.

There is limited literature regarding utilisation of FTPB, but three randomised trials comparing FTPB with TRB found no difference in the cancer detection rate between the two techniques . Furthermore, a meta-analysis, which included a further four case-control studies, again found no difference in the cancer detection rate between TRB and FTPB [10]. All seven studies compared various TRB protocols, from sextant biopsy through to saturation biopsy and they each compared the same number of cores from each technique.

But whilst cancer detection between FTPB and TRB appears to be equivalent, TTPB seems superior to TRB. Several studies have confirmed the utility of TTPBs in patients whom have had one or more negative TRBs. These series show cancer detection in up to 68% of patients, even when more than two previous TRBs have been negative [11]. In particular, anterior zone tumours are more readily detected on TTPB compared with a standard 12-core TRB. Additionally, TTPB is being used as a confirmatory biopsy in patients enrolled on active surveillance (AS) programmes, as it seems to provide more accurate staging than TRB alone [5].

A reasonable strategy, therefore, may be to perform all primary biopsies as FTPBs, either in the outpatient setting or in theatre in the lithotomy position under local anaesthesia with or without sedation. Our own experience has been with both local anaesthesia and sedation under which the procedure has been well tolerated. Repeat biopsies and particularly confirmatory AS biopsies could be performed with a grid template under general anaesthesia. And although pre-biopsy multiparametric MRI (mpMRI) is not yet mainstream practice, there is increasing evidence a pre-biopsy mpMRI may reduce unnecessary biopsies, allow clinicians to target suspicious lesions, minimise the number of cores required and follow patients on AS programmes without regular repeat biopsy. 'Cognitive' fusion FTPB may be possible, but would certainly require experience and probably the development of more effective 'freehand' needle guides.

Using a combination of both FTPB and TTPB would seem to strike the right balance between minimising the risk of sepsis, ensuring adequate cancer diagnosis and effective use of precious resources, but we need more data on the FTPB technique. This will only come when larger institutions explore this technique and publish their experience. It may not be time yet to phase out TRB altogether, but we should be proactive in searching for durable and effective solutions to the sepsis challenge that blunts our advocacy of PSA screening.

Conflicts of Interest

None disclosed.

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Correspondence: Philip Dundee, Department of Urology, Royal Melbourne Hospital, Grattam Street, Parkville, Vic. 3052, Australia.

e-mail: phildundee@gmail.com

Abbreviations: AS, active surveillance; mpMRI, multiparametric MRI; (F)(T)TPB, (freehand) (template-guided) transperineal biopsy; TRB, TRUS-guided biopsy of the prostate.

Radiation exposure to a pregnant urological surgeon — what is safe?

Angela M. Birnie and Stephen R. Keoghane

Department of Urology, Queen Alexandra Hospital, Portsmouth, Hampshire, UK

Introduction

The majority of theatre staff, 23% of urology trainees and 8.5% of urology consultants in the UK are female and often of childbearing age. It is common for female healthcare professionals to work during the first 16 weeks of pregnancy, statistically the time of greatest vulnerability for the foetus, despite a paucity of data relating to occupational surgical radiation during pregnancy [1]. In addition, many choose to disclose their pregnancy at a date beyond this time.

Radiation Exposure in Urology

During endourological procedures, radiation exposure is primarily due to scatter produced from interaction of the primary beam with the patient, operating table and floor. Most of the dose received by the surgeon during these procedures is via the lower limbs, hands and eyes, rather than the covered abdomen. Even with an annual caseload of 50 ureteric cases the dose received does not exceed 0.12% of the Ionising Radiations Regulation 1999 annual dose limit for adult workers [2].

Effect of Radiation on the Foetus

The bulk of data on the effects of radiation on the foetus is derived from ≈2800 pregnant survivors of the 1945 atomic bomb attacks on Hiroshima and Nagasaki. Of these, 500 received a radiation dose of 500–1000 mGray (mGy), far beyond the doses encountered in fluoroscopy [3]. The effects can be devastating and include organ malformation, growth restriction, severe mental retardation, childhood cancer and prenatal death [4]. They are influenced by the dose received by the foetus and its' developmental stage. Radiation-induced non-cancer side-effects are rarely detectable if the dose remains <50 mGy throughout pregnancy [5]. The rate of childhood cancer is 0.03–1.0% and the estimated lifetime cancer rate is 38–40% [6] in line with the general population.

The Gray (Gy) and Sievert (Sv): Units of Ionising Radiation

The gray (Gy) is a measure of the absorbed dose of ionising radiation and the severity of radiation poisoning. Radiation poisoning results from acute exposure to high levels of radiation and is certain to damage tissue (i.e. produce 'deterministic' effects). One gray is the absorption of one joule of energy in the form of ionising radiation per kilogram of matter. It is a physical quantity and is defined separately from the biological context. The sievert (Sv) is a measure of the health effect of a dose of low-level ionising radiation on human tissue and represents the probability of cancer induction and genetic damage (the 'stochastic' risk). It is weighted according to the type of radiation (e.g. X-rays, γ-rays, neutrons, protons) and, in partial or non-uniform body irradiation, the nature of each organ or tissue being irradiated. In relation to X-rays, one can assume for

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
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Title of Invention

METHOD, SYSTEM, AND DEVICE FOR PLANNING AND PERFORMING GUIDED AND FREE-HANDED TRANSPERINEAL PROSTATE BIOPSIES

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1007	FILED BY	Donna Carrera
PATENT CENTER #	60414882	FILING DATE	05/07/2021
CUSTOMER #	24030	FIRST NAMED INVENTOR	Matthew J. ALLAWAY
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Josh Pranckun

Documents

TOTAL DOCUMENTS: 35

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
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Digest

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UROLOGIC ONCOLOGY

Original Article

Free-hand transperineal prostate biopsy provides acceptable cancer detection and minimizes risk of infection: evolving experience with a 10-sector template

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Abstract

Introduction and Objectives: Free-hand transperineal prostate (fTP-Bx) biopsy offers an alternative to transrectal prostate biopsy (TRUS-Bx) in the diagnosis of prostate cancer. Our objectives were to determine whether fTP-Bx achieves cancer detection rates comparable to historic TRUS-Bx cohorts; to determine infectious and other complications associated with fTP-B; and to propose a standardized fTP-Bx template.

Patients and Methods: We present a single institution, retrospective review of fTP-Bx in 1,000 men with elevated prostate-specific antigen, abnormal digital rectal examination, or on an active surveillance protocol. A fan-like biopsy scheme was used in 883 patients. A 10-sector prostate biopsy template was developed for use in the final 117 patients. The primary outcome was detection of any cancer and detection of clinically significant cancer (Grade Group $\geq$ 2). Secondary outcomes included procedural specifics and complications. Chi Square and Mann-Whitney U were used for analysis of categorical and continuous variables, respectively.

Results: The median age of the cohort was 68 (interquartile range 61–74) years, and the median prostate-specific antigen was 7.9 (interquartile range 5.5–11.9) ng/ml. Total cancer (60.7%) and clinically significant cancer (40.3%) detection for fTP-Bx were comparable to those reported for TRUS-Bx. Detection of any cancer (70.9% vs. 59.3%, $P < 0.01$) and clinically significant cancer (51.3% vs. 38.9%, $P = 0.01$) was higher using the 10-sector biopsy template relative to the fan-like pattern. No patients were hospitalized for sepsis and no culture-proven urinary tract infections were diagnosed.

Conclusion: Cancer detection rates using fTP-Bx are comparable to TRUS-Bx, and fTP-Bx nearly eliminates the risk of infection. We propose a 10-sector biopsy template for fTP-Bx that easily translates to established MRI prostate sector maps for use in clinical care and future research studies exploring the efficacy of MRI-guided fTP-Bx. © 2018 Elsevier Inc. All rights reserved.

Keywords: Prostate biopsy; Prostate cancer; Transrectal ultrasound; Transperineal; Precision point; Complications

1. Introduction

In 2018, urologists in the United States will diagnose over 160,000 men with prostate cancer and will perform transrectal ultrasound-guided biopsies (TRUS-Bx) on many more [1,2]. TRUS-Bx was first popularized by Cooner in 1988 [3]. The technique was further refined by Stamey and colleagues who proposed the systematic sextant biopsy template in 1989 [4]. By the late 1990's, clinicians recognized that a sextant biopsy missed up to 30% of prostate cancers giving rise to the current standard of 10 to 12 core TRUS-Bx [5,6].

While most urologists in the United States continue to perform TRUS-Bx, this approach has several shortcomings. First, access to the entire prostate is limited. Clinicians often fail to adequately sample the apical and anterior

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regions of the prostate [7]. Second, infectious complications have been reported in up to 7% of patients with 3% requiring hospitalization [8]. Many expect these rates to rise as resistance to antimicrobials, particularly the commonly used fluoroquinolones, becomes more ubiquitous [9,10].

Free-hand transperineal prostate biopsy (fTP-Bx) offers an alternative approach. fTP-Bx allows easier access to all regions of the prostate, particularly the anterior and apical regions [11,12], and may more accurately predict clinical risk categories relative to TRUS-Bx [13]. Furthermore, infectious complications associated with fTP-Bx are exceedingly rare, with hospital admission rates for infection approaching zero [14,15]. Most clinicians are hesitant to adopt fTP-Bx due to unfamiliarity, perceived need for additional costly equipment (e.g. brachytherapy stepper and grid), assumed requirement for general anesthesia, and the absence of a standardized fTP-Bx template for outpatient use. We examined a large, outpatient fTP-Bx experience to determine the feasibility of this approach and the associated cancer detection rates.

2. Patients and methods

After obtaining Institutional Review Board approval, we performed a retrospective review of a prospectively collected single institution experience of 1,000 consecutive men undergoing fTP-Bx for elevated serum prostate-specific antigen (PSA) level ($\geq$ 4.0 ng/ml), abnormal digital rectal examination, or on an active surveillance protocol from April 2011 to December 2017. Three urologists (M.A., J.R., and V.P), each with greater than 5 years experience in TRUS and fTP-Bx performed the biopsies. For men who underwent multiple fTP-Bx ($n = 116$), only the initial biopsy was included in the analysis. Patients with a prior history of prostate cancer treatment (e.g. external beam radiation or brachytherapy) were excluded. For men who underwent a prebiopsy MRI ($n = 202$), only the template-based biopsies were included in the analysis. Information concerning patient demographics, clinical care, and complications was collected prospectively and recorded in a database.

All procedures were performed in an outpatient surgery center. For the majority of patients ($n = 873$), intravenous sedation was administered. With experience, sedation was omitted in favor of local anesthesia alone ($n = 127$). Early in the cohort, a single dose of cephalexin was administered. In the last 400 patients, no antibiotic prophylaxis was administered. Alpha-blocker therapy was not utilized unless patients were already taking the medication. Complications were graded using the Clavien-Dindo classification system [16].

2.1. Patient positioning

Men were positioned in the dorsal lithotomy position. The scrotum was elevated away from the perineum and secured with tape (Fig. 1). The skin was cleansed using 2% chlorhexidine gluconate in 79% isopropyl alcohol (BD, Franklin Lakes, NJ). A bi-plane, side-fire, ultrasound probe (8848 BK, Cambridge MA) was inserted into the rectum. Prostate size was estimated using traditional height, width, and length measurements.

2.2. Access point location and local anesthetic block

Perineal anesthesia can be accomplished using several methods [17]. We used an access point estimated as the midpoint between the midline and the far lateral edge of the prostate on each side. The height of the access point was approximately half the distance from the posterior to the anterior capsule. The anesthetic block was initiated by raising a skin wheal with buffered 1% lidocaine at the access point and continued from the skin to the pelvic floor muscle using a 6", 20-gauge spinal needle. Once inside the pelvic floor muscle, a bolus of 5 to 7 ml was injected and observed tracking around the anterior and posterior capsules. The final 5 to 7 ml bolus was insinuated between the apical capsule and the submuscular pelvic floor (Fig. 1a). This procedure was repeated on each side. Approximately 20 to 30 ml of 1% lidocaine with 3 ml bicarbonate was used to accomplish the block.

2.3. Prostate biopsy technique

All biopsies were performed using the Bard 18-gauge disposable biopsy device (Bard Biopsy Systems, Tempe, AZ). For the initial series of men ($n = 883$) biopsies were performed in a "fan-like" pattern [18]. A 14-gauge hypodermic needle was inserted through an access point to the left and right of the midline and utilized as a re-entry conduit. Subsequently, the PrecisionPoint Transperineal Access System (Corbin Clinical Resources, Cumberland MD) was developed and utilized ($n = 117$). This technique employs an access needle mounted to a carriage with multiple apertures. The device is coupled to the ultrasound probe so that all trajectories of the biopsy needle are aligned with the sagittal imaging plane. The probe is manipulated, in a freehanded fashion, fine-tuning the position of the access needle to satisfy the desired trajectory of the biopsy needle (Fig. 1b). Biopsies were performed according to a 10-sector template (Fig. 2) that corresponds to the prostate sector map utilized in PIRADS v2 (Fig. 3) [19].

2.4. Statistical analysis

Prostate volume was calculated using the ellipsoid volume calculator (L*W*H*Π/6). PSA density was calculated as the PSA level divided by prostate volume. Clinically significant cancer was defined as Grade Group 2 or higher. Chi square testing was used to test for differences between categorical variables. The Mann-Whitney U test was used to compare continuous variables. A P-value < 0.05 was considered statistically significant.

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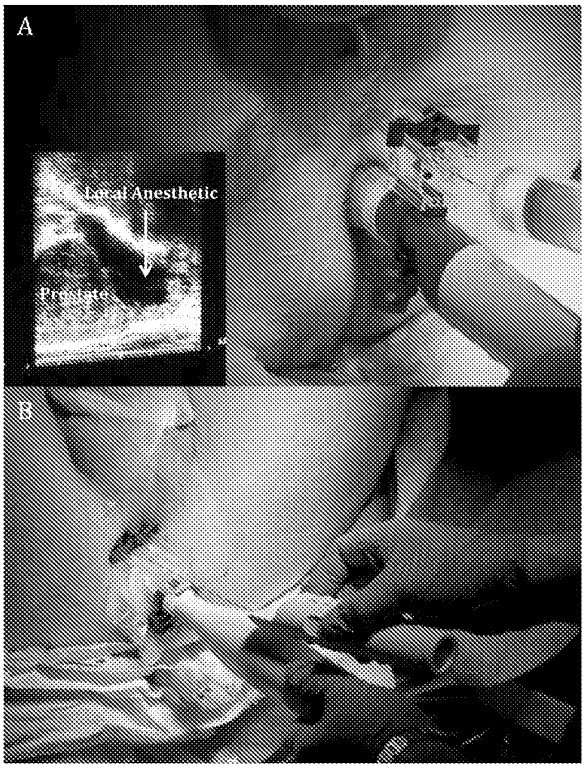


Fig. 1. (A) Local anesthetic block technique; ultrasound image demonstrates local anesthetic surrounding the apical prostate; (B) Free-hand transperineal prostate biopsy using the precision point transperineal access system (Corbin Clinical Resources, Cumberland MD).

3. Results

3.1. Patient and procedural characteristics

A total of 1,000 men underwent fTP-Bx (Table 1). The median age of the cohort was 68 years (interquartile range [IQR] 61 to 74), and most men (96%) were Caucasian. The median PSA and prostate volume were 7.9 (IQR 5.5 to 11.9) ng/ml and 41.8 (IQR 29.3 to 58.1) cm^3, respectively. Fifty-one men (5.1%) who underwent prostate biopsy had an abnormal digital rectal examination. There was no difference in PSA density (0.19 vs. 0.18 ng/ml/cm^3, $P = 0.09$), percent on active surveillance (30.4% vs. 23.1%, $P = 0.11$), or MRI use (19.5% vs. 25.6%, $P = 0.12$) between patients undergoing biopsy using the fan-like fTP-B technique

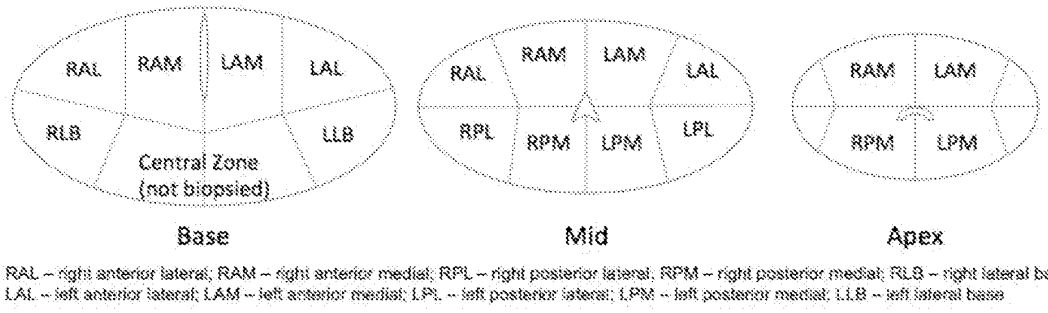


Fig. 2. Transperineal prostate biopsy: 10-sector template.

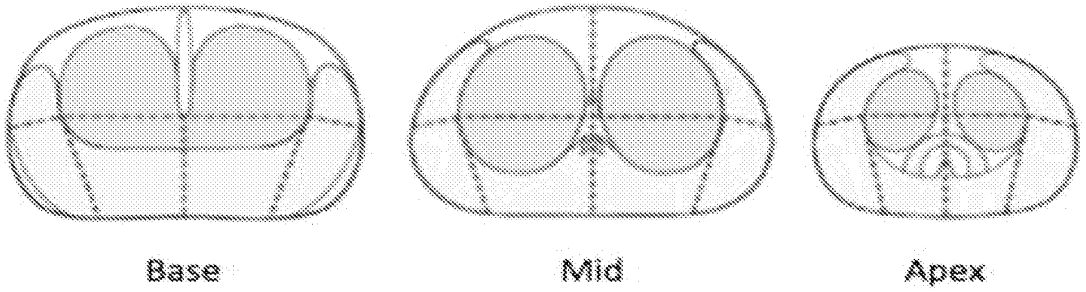


Fig. 3. Prostate MRI sector map. *modified with author permission from Moore et al. Eur Urol 2017; 71:648–55

versus the 10-sector approach. Mean procedural time was 11.2 ± 6.1 minutes throughout the study period.

3.2. Cancer detection

The median number of cores per prostate biopsy was 16 (IQR 14 to 20). Overall cancer detection for the study cohort was 60.7% (Table 2). Total cancer detection for patients who underwent fTP-Bx using the 10-sector approach was greater than those in whom a fan-like pattern was used (70.9% vs. 59.3%, $P < 0.01$). Similarly, detection of Gleason Grade Group ≥ 2 was higher using the 10-sector fTP-Bx technique relative to the fan-like pattern (51.3% vs. 38.8%, $P = 0.01$).

Cancer detection by sector for patients undergoing biopsy using the 10-sector approach is listed in Table 3. No statistically significant difference in cancer detection by sector was observed ($X^2 = 13.203$, $P = 0.15$).

3.3. Complications

In 1,000 patients, there were no culture-proven urinary tract infections and no hospital admissions for sepsis of urologic origin. Three patients (0.3%) were prescribed antibiotics for lower urinary tract symptoms in the absence of a culture-proven urinary tract infection (Clavien-Dindo II). One patient (0.1%) developed urinary retention (Clavien-Dindo I). No patient developed hematuria requiring catheter placement or surgical intervention. Patients did not require pain medication postprocedurally.

4. Discussion

For nearly 20 years, urologists have recommended a 10 to 12 core TRUS-Bx for men undergoing a prostate biopsy [20]. Problems with this approach include difficultly sampling the anterior and apical regions of the prostate and the risk of sepsis. Based upon data derived from an analysis of the largest reported series of outpatient fTP-Bx to date, we believe that fTP-Bx is acceptable to patients and urologists, enables equivalent cancer detection rates when compared to traditional TRUS-Bx, and reduces procedure-associated complications.

Cancer detection in the cohort was 60.7% overall and 40.3% for clinically significant (GG ≥ 2) disease. This compares favorably with historical 10-12 core TRUS-Bx cohorts in which overall cancer detection rates range from 40.3% to 44.4% [6,21]. Moreover, these rates are similar to

Table 1
Demographic and baseline clinical information for TP-Bx patients

	Fan-like technique ($n = 883$)	10-sector technique ($n = 117$)	P	Total cohort ($n = 1000$)
Median age (IQR), y	67 (61–74)	70 (63–75)	0.07	68 (61–74)
Race, *n* (%)				
Caucasian	851 (96.4%)	109 (93.2%)	0.10	960 (96%)
African-American	32 (3.6%)	8 (6.8%)		40 (4%)
Median BMI (IQR), kg/m^2	28.3 (25.5–31.5)	28.7 (25.0–32.2)	0.93	28.3 (25.5–31.5)
Median PSA (IQR), ng/ml	7.9 (5.5–11.9)	8.7 (5.1–12.5)	0.30	7.9 (5.5–11.9)
Median prostate volume (IQR), cm^3	41.7 (29.3–58.2)	42.5 (29.3–56.0)	0.87	41.8 (29.3–58.1)
Median PSA density (IQR), ng/ml/cm^3	0.19 (0.12–0.31)	0.18 (0.11–0.28)	0.09	0.19 (0.12–0.31)
Prior TRUS-Bx, *n* (%)	226 (25.6)	37 (31.6)	0.16	263 (26.3%)
Prior MRI, *n* (%)	172 (19.5)	30 (25.6)	0.12	202 (20.2%)
Patients on active surveillance, *n* (%)	268 (30.4)	27 (23.1)	0.11	295 (29.5%)

Table 2
Pathological outcomes for TP biopsy by approach.

	Fan-like technique ($n = 883$), n (%)	10-Sector technique ($n = 117$), n (%)	Total ($n = 1000$), n (%)
Benign	359 (40.7)	34 (29.1)	393 (39.3)
Grade Group 1	181 (20.5)	23 (19.7)	204 (20.4)
Grade Group 2	149 (16.9)	28 (23.9)	177 (17.7)
Grade Group 3	93 (10.5)	10 (8.5)	103 (10.3)
Grade Group 4	37 (4.2)	8 (6.8)	45 (4.5)
Grade Group 5	64 (7.2)	14 (12.0)	78 (7.8)

Table 3
Cancer detection by sector for the 10-sector template.

Sector	Cancer detection (%)	Clinically significant cancer detection (%)
Right lateral base	33 (28.2)	23 (19.7)
Right anterior lateral	32 (27.4)	19 (16.2)
Right anterior medial	34 (29.1)	17 (14.5)
Right posterior lateral	45 (38.5)	26 (22.2)
Right posterior medial	45 (38.5)	29 (24.7)
Left lateral base	30 (25.6)	17 (14.5)
Left anterior lateral	27 (23.1)	14 (12.0)
Left anterior medial	31 (26.5)	8 (6.84)
Left posterior lateral	45 (38.4)	27 (23.1)
Left posterior medial	39 (33.3)	21 (17.9)

those obtained in the PROMIS study (71% for overall cancer detection and 57% for GG $\geq$ 2 disease), which used a transperineal template prostate mapping biopsy technique [11]. Reports suggest that the incidence of Gleason Grade upgrading at radical prostatectomy does differ by biopsy approach (30.4% for TP-BX vs. 33.2% for TRUS-Bx); however, TP-Bx may provide greater accuracy in predicting final clinical risk category relative to TRUS-Bx [13].

Complications associated with fTP-Bx in this cohort were rare. No culture-documented urinary tract infections occurred and no patient required hospitalization for sepsis. These results were achieved using either a single dose of cephalexin or no antibiotics. Others have reported a similarly low or nonexistent infectious risk using the TP-Bx approach [14,22]. In contrast, the risk of infection for patients undergoing TRUS-Bx is high. While rectal swab, culture-directed antibiotic prophylaxis has mitigated some of these challenges [23] increasing resistance to antimicrobials is unavoidable. Elimination of antibiotic prophylaxis with no increase in infectious risk remains a major advantage to the fTP-Bx approach.

To date, outpatient fTP-Bx lacks a standard template. Using an access device that permitted an accurate 10-sector template sampling procedure, we achieved a cancer detection rate comparable to the traditional TRUS-Bx technique. A major advantage of the 10-sector template is the ease with which it translates to established MRI prostate sector maps (Fig. 3) thereby facilitating MRI-directed biopsies. Clinicians have increasingly incorporated MRI imaging into active surveillance protocols and have recommended MRI testing for patients with persistently elevated PSA after a negative biopsy [24, 25]. In addition, recent data have demonstrated the utility and cost-effectiveness of upfront prostate MRI in biopsy naïve patients [26, 27]. Therefore, the ability to translate MRI sector maps easily to biopsy templates is critical. Although MRI/US fusion-targeted fTP-Bx is beyond the scope of the present study, the PrecisionPoint device is capable of integrating with commonly used MRI/US fusion software. Establishment of a standard fTP-Bx template is an essential first step, since it will facilitate future MRI/US fusion-targeted fTP-Bx research.

Limitations of our study include its retrospective design and accrual within a single institution. This may limit its applicability to other populations. Second, the study population is primarily Caucasian potentially limiting generalizability to other racial groups. Third, the number of biopsy cores was not standardized since the optimal number and location of biopsy cores has yet to be determined. Differences in the number of cores obtained may impact the incidence of prostate cancer identified by fTP-Bx. Fourth, patients who are on active surveillance or those with prebiopsy MRI may influence the number and location where urologists perform biopsies. However, there were no differences in the proportion of patients on active surveillance or with prebiopsy MRI between the two fTP-Bx techniques. Finally, there is no direct TRUS-Bx control group with which to make comparisons since we began collecting data when fTP-Bx was introduced at our institution. Still, we believe that comparison to historical controls provides adequate equipoise for further investigation between the TRUS-Bx and fTP-Bx approaches.

5. Conclusions

To our knowledge, we report the largest cohort of men undergoing outpatient fTP-Bx. Cancer detection rates are comparable to traditional TRUS-Bx, and the fTP-Bx approach eliminates the need for antibiotic prophylaxis. We propose a 10-sector template that facilitates fTP-Bx and easily translates to established MRI prostate sector maps for use in clinical care and future research studies exploring the efficacy of MRI-guided fTP-Bx.

Conflicts of interest statement

Matthew Allaway is the CEO and Founder of Perineologic. John Hart is the Director of Operations for Perineologic. The remaining authors have nothing to disclose.

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Author roles and contributions using the CRediT taxonomy

Conceptualization: BTR, MA, PCA
Methodology: BTR, MA, PCA
Formal Analysis: BTR, PCA
Investigation: MA, DC, JH, JR, VP
Data Curation: BTR, MA, DC, JH
Writing—Original Draft: BTR, PCA
Writing—Reviewing and Editing: BTR, MA, DC, JH, JR, VP, PCA
Supervision—MA, PCA

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HOYNG ROKH MONEGIER

SUMMONS IN INTERLOCUTORY PROCEEDINGS

WITH SHORTENING OF THE SUMMONS PERIOD EX ART. 117 RV

CONCERNING INFRINGEMENT OF THE EUROPEAN PATENT EP (NL) 3 125 811 B1

This twenty-first day of October two thousand and twenty-one (21-10-2021), at the request of **CORBIN CLINICAL RESOURCES LLC (**hereinafter: "**Corbin**"), a company incorporated and having its registered office in Cumberland, MD, United States of America, (U.S.A.), with an address for service in this matter at HOYNG ROKH MONEGIER B.V, in (1096 HA) Amsterdam, at Amstelplein 1 (Rembrandt Tower, 30th floor), at the offices of the lawyers S.C. Dack and P. van Schijndel, who will appear for Corbin in these proceedings and will be identified as such;

I

By virtue of an order given by the Preliminary Relief Judge of the District Court of The Hague on 20 October 2021, a copy of which is being served together with this writ, whereby Corbin was granted leave to summon in accordance with Rule 117 of the Dutch Code of Civil Procedure,

SUMMARILY SUMMONSED

WITH SHORTENING OF THE SUMMONS PERIOD EX ART. 117 RV:

1. The Dutch company with limited liability **PELVITEC B.V.** ("**Pelvitec**") with registered office at Rotterdamseweg 183-C, 2629 HD in Delft, choosing for the purposes of the present proceedings its place of domicile Lange Voorhout 3, 2514 EA The Hague, at the offices of BARENTS KRANS N.V., of which law firm Mr. J. Bremer will appear as lawyer for Pelvitec, at that address

   [ ] serving a copy of this writ on

working there;

[ ] leaving behind at the aforementioned address this writ in a closed envelope with the statements as prescribed by law because I did not find anyone there to whom a legally valid copy could be left;

2. The company under foreign law **LEAPMED FRANCE SAS** ("**Leapmed**"), which has no known office address in the Netherlands, but a known address at 5 Chemin de Laborie, 31560 Nailloux in France.

In making this notification, I have observed the method of service pursuant to Regulation (EC) No 1393/2007 of the European Parliament and of the Council of 13 November 2007 on the service in the Member States of judicial and extrajudicial documents in civil or commercial matters (the 'Service Regulation') in conjunction with Article 56 of the Code of Civil Procedure, as follows:

(i) I have sent two copies of this writ, as well as translations thereof in the French language, for service on the defendant to the receiving agency in the country in which the defendant's address is situated, namely:

SCP Terrin Vallien Bendenoun Barthe
3 Place du Foirail
31800 SAINT-GAUDENS
France

(ii) The form referred to in Article 4(3) of the aforementioned Regulation has been completed by me, the judicial officer, in the French language, which is the official language of the place where service is to be effected. I request the receiving agency to serve this document on the defendant / to notify the defendant as described at point 5 in the request for service of documents form, i.e. service in accordance with the law of the State addressed (form, 5.1);

(iii) I have also sent a copy of this writ together with a French translation thereof and the form provided for in Article 8 (1) of the Regulation on Names and Distinctions by FedEx direct and by registered post (with acknowledgement of receipt) to the above address of LEAPMED FRANCE SAS, stating that receipt of this document may be refused if it is not written in or accompanied by a translation into French or a language that the claimant understands, and that in the event of refusal the documents and the completed form must be returned to me, the judicial officer, within one week;

3. the company under American law **ADVANCE MEDICAL DESIGNS INC**., having its registered office at 1241 Atlanta Industrial Drive, Marietta GA 30066, with no known place of business or residence in the Netherlands, choosing for the purposes of the present proceedings its place of domicile Lange Voorhout 3, 2514 EA The Hague, at the offices of BARENTS KRANS N.V., of which law firm Mr. J. Bremer will appear as lawyer for Advance Medical Designs Inc,, at that address

   [ ] serving a copy of this writ on

   working there;

   [ ] leaving behind at the aforementioned address this writ in a closed envelope with the statements as prescribed by law because I did not find anyone there to whom a legally valid copy could be left;

4. The natural person **NICO EELBODE**, general manager and owner of the company MEPY BENELUX, with registered office at Zeedijk 130 8400 Ostend, Belgium and also owner and manager of the French company MEDKONSULT SARL, with registered office at 5 CHE DE LABORIE 31560 NAILLOUX, France

   As regards the office address in Belgium known to Mr Eelbode:

   (a) In making this notification, I have observed the method of service pursuant to Regulation (EC) No 1393/2007 of the European Parliament and of the Council of 13 November 2007 on the service in the Member States of judicial and extrajudicial documents in civil or commercial matters (the 'Service Regulation') in conjunction with Article 56 of the Code of Civil Procedure, as follows:

      (i) I have sent two copies of this writ for service on the defendant to the receiving agency in the country in which the defendant's address is located, namely:

      National Chamber of BailiffsHenri
      Jaspar Avenue 931060
      BrusselsBELGIUM

(ii) The form referred to in Article 4(3) of the aforementioned Regulation has been completed by me, the court bailiff, in the Dutch language, which is an official language of the place where service is to be effected. I have requested the receiving agency to serve this notice on the defendant / to notify the defendant as described at 5 in the aforementioned form "request for service of documents", namely service in accordance with the law of the State addressed (form, 5.1);

(iii) I have also sent a copy of this writ, as well as the form within the meaning of article 8 (1) of the Service Regulation, directly by FedEx and by registered post (with acknowledgement of receipt) to the aforementioned address of MEPY Benelux for the attention of Nico Eelbode, with the statement that receipt of this document may be refused if it is not written in Dutch and that in the event of refusal the documents as well as the completed form should be returned to me, the court bailiff, within one week;

As regards the office address in France known to Mr Eelbode:

(b) In making this notification, I have observed the method of service pursuant to Regulation (EC) No 1393/2007 of the European Parliament and of the Council of 13 November 2007 on the service in the Member States of judicial and extrajudicial documents in civil or commercial matters (the 'Service Regulation') in conjunction with Article 56 of the Code of Civil Procedure, as follows:

(i) I have sent two copies of this writ, as well as translations thereof in the French language, for service on the defendant to the receiving agency in the country in which the defendant's address is situated, namely:

SCP Terrin Vallien Bendenoun Barthe
3 Place du Foirail31800
SAINT-GAUDEN France

(ii) The form referred to in Article 4(3) of the aforementioned Regulation has been completed by me, the judicial officer, in the French language, which is the official language of the place where service is to be effected. I request the receiving agency to serve this document on the defendant / to notify the defendant as described at point 5 in the request for service of documents form, i.e. service in accordance with the law of the State addressed (form, 5.1);

(iii) I have also sent a copy of this writ together with a French translation thereof and the form provided for in Article 8(1) of the Regulation on Names and Numbers, by FedEx and by registered post (with acknowledgement of receipt) direct to the aforementioned address of SARL Medkonsult, stating that receipt of this document may be refused if it is not

written in or accompanied by a translation into French or a language that the claimant understands, and that in the event of refusal the documents and the completed form must be returned to me, the judicial officer, within one week;

IN ORDER TO:

Appear on **TUESDAY THE SECOND OF NOVEMBER TWO THOUSAND AND TWENTY-ONE (02-11-2021), at nine o'clock in the morning (9:00 a.m.)**, in person or represented by an attorney, at the hearing before the judge in preliminary relief proceedings of the District Court of The Hague on duty at that time in the case / docket number 619229 / 21-974, which hearing will take place on the said date and time at the District Court of The Hague in the Palace of Justice, Prins Clauslaan 60, 2595 AJ The Hague;

Whereby a digital hearing will be held on **TUESDAY THE THIRTIETH OF NOVEMBER TWO THOUSAND AND TWENTY-ONE (30-11-2021) at nine o'clock in the morning (09:00 a.m.)**;

UNDER NOTICE THAT:

a. If a defendant does not appear in person or represented by a lawyer at the hearing and the prescribed time limits and formalities have been complied with, the court will grant default judgment against that defendant and allow the claim set out below, unless it deems it to be unlawful or unfounded;

b. if at least one of the defendants has appeared in person or with a lawyer at the hearing, a single judgment will be rendered between all the parties, which will be regarded as a judgment after trial;

c. in the event that each of the defendants appears in court, a court registry fee will be charged, to be paid within four weeks from the time of appearance;

d. the amount of the court fee is stated in the most recent annex to the Civil Cases Court Fees Act, which can be found on the website: www.kbvg.nl/griffierechtentabel

e. a court fee for impecunious persons fixed by or pursuant to the law shall be levied on a person who is impecunious, if he has submitted a copy of the application at the time when the court fee is levied:

i. a copy of the decision to grant legal aid, as referred to in section 29 of the Legal Aid Act, or if this is not possible due to circumstances which cannot reasonably be attributed to him, a copy of the application as referred to in section 24, second paragraph, of the Legal Aid Act; or

ii. a statement from the Board of the Legal Aid Board, as referred to in section 7(3)(e) of the Legal Aid Act, showing that his income does not exceed the incomes referred to in the Order in Council under section 35(2) of that Act;

f. defendants who appear before the same lawyer and submit identical submissions or put forward identical defences, only one joint court fee is charged on the basis of Article 15 of the Civil Cases (Court Fees) Act;

AND NOTING THAT:

The judge in preliminary relief proceedings of the District Court of The Hague ruled as follows in her order of 20 October 2021:

"Contents of writ

1. Claimant must set the date for defendant's appearance in the writ as **Tuesday, November 2, 2021, at 9:00 a.m**.
2. The summons must state that the case will be heard by the judge in charge of preliminary relief proceedings at that time.
3. The claimant shall include his/her own e-mail address and telephone number in the writ of summons. To the extent known to him, the claimant shall also include the defendant's e-mail address and telephone number in the summons.
4. The writ should also include that a digital hearing will take place on **Tuesday, November 30, 2021 at 9:00 a.m**.
5. A copy of this document must be served on the defendant together with the writ.

Method of appearance

6. If the plaintiff has not withdrawn the application for interim relief before the date on which the defendant must issue a statement of defence (i.e. the date mentioned above under 1), the plaintiff shall be deemed to have appeared by submitting the issued as issued to the court registry.
7. Appearance by the defendant is effected by submitting a statement of defence (including exhibits) on the date mentioned in item 1 above. If the defendant so desires, he/she must also lodge a counterclaim no later than on this date.
8. If the defendant fails to submit a statement of defence, in principle - if the prescribed time limits and formalities have been observed - default judgment will be granted against the defendant.

Submission of exhibits, pleadings and response to pleading of plaintiff by defendant

9. Purely reactive claimant's exhibits (i.e. exhibits in response to submissions made by the defendant in its defence) may be submitted by **Tuesday, 16 November 2021 at 9.00 a.m**. If

the defendant has submitted a counterclaim, the plaintiff must also submit a defence to the counterclaim on this date.

10. Subsequently, the defendant may submit purely reactive exhibits (i.e. only exhibits in response to the claimant's reactive exhibits) no later than 24 hours before the submission of the written pleading (see point 13 below), therefore on **Tuesday 23 November 2021 at 9.00 a.m.**
11. Both parties shall submit a written pleading no later than **9:00 a.m. on Friday, November 26, 2021**.
12. Pleadings must be (excluding the cover page with the parties' names) a maximum of 30 pages (maximum 9,000 words) and must be written in a customary (clearly legible) font and layout. For the defendant a maximum of 30 pages (maximum 9,000 words) applies as well, on the understanding that the defendant, if so desired, can reserve a maximum of 5 pages (1,500 words) for a written reaction to the plaintiff's memorandum of law (see below under item 14 [*sic*: must be: 13]).
13. Defendant may submit a brief (maximum 5 A4) written response to Plaintiff's pleading on **Monday, November 29, 2021, at 9:00 a.m.**
14. If the parties wish to submit an updated overview of the legal costs, they must do so in accordance with the Indication Tariffs in IP cases and submit it to the court in preliminary relief proceedings and to the other party not later than 24 hours before the start of the digital hearing. During the digital hearing, the parties will have the opportunity to respond to the costs of the proceedings.
15. Written pleadings and exhibits are sent to the registry of the court with cc to (the lawyer of) the other party via the following e-mail address: (kortgeding.ie.rb.denhaag@rechtspraak.nl). All documents to be submitted must comply with the requirements set out in the Instructions for the submission of documents in IP cases, whereby exhibits 1 to 9 must be numbered with a 0 before them (EP01, EP02, etc / GP01, GP02 etc).

Digital hearing by connection via Skype for Business

Prior to the session

16. On the date and time mentioned under point 5, a digital hearing will be held, in principle by means of a connection via Skype for Business. This hearing is meant for reply and rejoinder (i.e. the parties are allowed to respond to each other's positions) of 2 x 10 minutes, for questions by the interim relief judge, and to see whether a settlement is possible.
17. Parties will receive an invitation to participate in the digital hearing, in principle one week before the hearing date. This invitation contains a link with which the participants can dial in to the digital hearing.
18. One invitation per party will be sent to the e-mail address supplied to the court. The link included in the invitation can be shared with third parties (lawyers/parties/other third parties) that are required to be present at the hearing, so that they can participate in the hearing with their own digital connection. They can use the same link to dial in.
19. The parties are requested to provide the names (and where relevant the function) of all persons who will participate in the digital hearing no later than one week before the digital hearing.
20. All information required to use Skype for Business can be found through the following link: https://www.rechtspraak.nl/coronavirus-(COVID-19)/Pages/COVID-19-Online-sessions-and-consultations.aspx
21. Parties must download the required programs in a timely manner if they wish to participate in the digital session via Skype for Business.
22. A party in need of a test of the connection may request it through the Clerk's Office.

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The meeting: general

23. At the digital hearing, the lawyers of the parties and the parties themselves are present. This can be done at the lawyers' offices. If it is not possible for a party to participate in the digital hearing at the office of his/her lawyer, that party can participate independently by using a separate digital connection. Of course, a defendant who litigates without a lawyer can do so as well.
24. If participants require the use of an interpreter, the parties shall make their own arrangements for a separate connection between the interpreter and the participant. The interpreter and the participant may both dial into the meeting (with the microphone turned off) where the interpreter can translate through the separate connection.
25. In principle, the interim judge and the registrar will wear a toga during the digital hearing."

IN ORDER:

Then to hear and determine the following claims:

Introduction

1. With only one or two exceptions, most of the patent cases heard by the District Court of The Hague in recent years have concerned minor improvements to existing products or processes, conceived by teams of inventors, often working in densely-populated technical fields, producing patents for large corporations with patent portfolios sometimes measured more in terms of volume than quality. We refer to the plethora of formulation and process patents in the pharmaceutical field; and to the many cases of *standard essential patents* in the electronics field.

2. That is not to say that such patents do not contain inventions: it is well known that the level for inventive step at the EPO is low. However, it is rare for patent litigators (or, we suspect, patent judges) to be truly impressed by the degree of innovation, or the elegant simplicity, of the inventions in the patents they are called to litigate (or decide upon).

3. The present case is a welcome exception to the general rule.

4. The patentee, Corbin, is a company formed by the inventor, Dr. Matthew Allaway, to exploit the intellectual property rights to his invention. Dr. Allaway is a urologist. His practice is particularly focused on the treatment of prostate cancer.

5. The present case concerns the infringement by the defendants of EP (NL) 3 125 811 (here 'EP 811', **Exhibit 1**[1]), which relates to a medical device invented by Dr Allaway that is used to take prostate biopsies.

6. It is no exaggeration to say that the commercial implementation of the patent – the medical device known as the *PrecisionPoint™ Transperineal Access System*, has quickly revolutionized prostate biopsy procedures.

   For more details of the device, reference is made to https://perineologic.com/precisionpoint/ and to an animation on YouTube describing the use of the device: https://www.youtube.com/watch?v=vV60sUQexuE.

7. Dr. Popert is one of the most eminent and respected consultant urologists in the UK. He was closely involved in the introduction of the device into clinical practice in the UK. He has prepared a report for the present procedure (**Exhibit 5**).

8. In his report, he discusses the drawbacks of the two conventional prior art techniques that were used to take prostate biopsies at the priority date of the patent. He explains how the introduction of the patented PrecisionPoint™ device in 2018 fundamentally changed the way urologists in the UK perform prostate biopsies. Reference will be made to his report in the following, which should be considered repeated and incorporated herein in its entirety.

9. Introducing the device to the UK and European markets required significant investment in the training of urologists and specialist nurses[2]. In the U. K., the PrecisionPoint™ device quickly became the gold standard for prostate biopsies. It is estimated that today around 65% of all prostate biopsies in the U. K. are performed using the PrecisionPoint™ device.

10. The device was also initially successful in The Netherlands, due to carefully planned training and mentoring programs for Dutch urologists and hospitals. Reference is made to the statement of Mr. Wilco Van der Lugt of BXTA (**Exhibit 7**). BXTA is the exclusive distributor for the patented PrecisionPoint™ device in Europe.

11. Recently, however, the defendants realized that a device they market, the SureFire, can easily be adapted to make it into a device that comes within the scope of protection of EP 811. The modified SureFire device enjoys the substantial benefits of the invention as a result of the modification.

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[1] An extract from the Dutch register showing that the patent is in force in the Netherlands is attached as **Exhibit 2**. The Dutch claims can be found in **Exhibit 3**. Excerpts from the granting history at the EPO are included in **Exhibit 4**.

[2] This is set out in the witness statement of Mr Saheed Rashid (**Exhibit 6**), whose company, BXTA, is the exclusive distributor of the patented device in, inter alia, the Netherlands.

The role of the various defendants

12. Defendant sub 1, Pelvitec B.V., is the Dutch distributor of the SureFire device. As will be discussed in more detail below, Pelvitec provides explicit instructions, which deviate from the official IFU for the SureFire, which bring the SureFire device within the scope of protection of the patent.

13. Defendant sub 2 (LeapMed France) is the European subsidiary of the Chinese manufacturer LeapMed. Its name and address are mentioned on the promotional material with which the device is (or until recently was) offered on the Dutch market and on the IFU (*Instructions for Use*) that were be sent by Pelvitec to (potential) customers in September 2021[3]. The company name LeapMed is also displayed on the SureFire device itself.

14. Defendant sub 3 (AMD Inc.) is an American company whose name is printed on the sticker on the sterile packaging of a LeapMed device recently found on the Dutch market. The packaging states that production takes place in China (where LeapMed France's parent company is located) and that the sterile packaging is subsequently done in America by AMD.

15. According to Pelvitec, AMD is the source of the SureFire devices which it puts on the Dutch market[4]. On the website of AMD there is a film showing that it too is also promoting an infringing adaptation of the SureFire device[5].

16. There is currently some uncertainty as to the precise roles of Defendants sub 2 and 3. The promotional material sent out by Pelvitec to potential customers suggests that LeapMed France (defendant sub 2) is the *Authorized European Representative* for the manufacturer (and that the manufacturer of the device is the Chinese parent company, LeapMed).

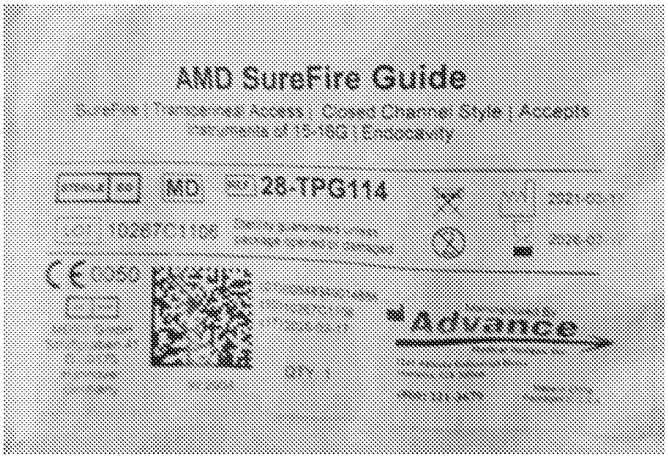
17. On the other hand, the sticker on the device recdently found on the Dutch market suggests that the manufacturer is AMD, and that the European representative of AMD is the commercial representation company MDSS GmbH:

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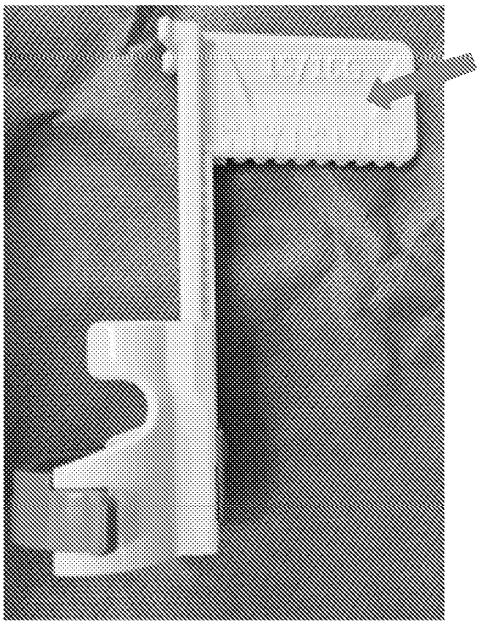
[3] See **Exhibit 7**.

[4] This is inconsistent with the fact that LeapMed France is listed on the IFU that Pelvitec sent to hospitals in September 2021.

[5] See https://www.advancemedicaldesigns.com/category/transperineal-biopsy/transperineal-biopsy, which links to https://www.youtube.com/watch?v=VACZrtejkNU. The video shows how AMD suggests using the SureFire along with a coaxial needle.



18. However, the device inside the packaging still bears the name LeapMed, molded into the product itself:



19. Defendant sub 4, Mr Eelbode, is (or, according to him: was) employed by LeapMed in Europe. He is involved in these proceedings because it appears from correspondence with him that he possesses essential information about the infringing practices of both LeapMed France and AMD. With respect to Mr Eelbode, Corbin is claiming specific disclosure pursuant to art. 843a Rv, in

order to have sight of documents pertaining to the infringing marketing of the LeapMed SureFire device by the other defendants and/or by Mr Eelbode himself (and/or by one of Mr Eelbode's companies).

Patent infringement by Pelvitec, LeapMed France and AMD

20. Corbin takes the view that Pelvitec, Leapmed France and AMD, each on its own and together, by supplying to hospitals and urologists in the Netherlands means relating to an essential element of the patented invention to third parties for the purpose of putting the invention into effect in The Netherlands (i.e. in order to turn it into an apparatus falling within the scope of protection of the claims of EP 811), and by instructing and encouraging hospitals and urologists to make and use the infringing apparatus, without the permission of the patent holder, are committing acts of indirect patent infringement under of article 73 ROW 1995.

21. By encouraging and promoting patent infringement by third parties and by profiting from it Pelvitec, Leapmed and AMD are also acting tortiously towards Corbin.

22. Corbin wishes to put an end to the infringement by - and the unlawful actions of - these defendants. It is therefore seeking an injunction declared provisionally enforceable, supported by penalty payments, and other measures, including a recall order, an order for rectification and an audit report, in order to be able to establish the scale of the infringement and to identify the sources and distribution channels of the infringing devices.

The patent

23. EP 811 is directed to an apparatus for performing transperineal prostate biopsies.

24. As Dr. Popert explains in his expert report[6], prostate cancer is the most common cancer in men.

25. A prostate biopsy is indicated when a blood test for prostate specific antigen (PSA) or a digital rectal examination performed by the urologist reveals irregularities that may indicate prostate cancer[7].

26. A prostate biopsy involves taking a number of tissue samples from the prostate[8]. In about half of the cases, the biopsy will detect the presence of prostate cancer[9].

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[6] See **Exhibit 5**.

[7] See EP 811, para. [0003].

[8] See EP 811, para. [0003].

[9] See Dr Popert's expert report (**Exhibit 5**), para 30.

27. As of the priority date of the patent, there were essentially two conventional methods for performing biopsies, namely the transrectal ultrasound-guided procedure (the *TRansrectal UltraSound* biopsy, or "TRUS") and the transperineal ultrasound-guided procedure (the *TRansperineal UltraSound* biopsy, or "TPUS") [10].

The problems with conventional transrectal (TRUS) biopsy procedures

28. As explained in the patent[11], and as Dr. Popert set out[12] in his report, the disadvantage of the transrectal method is that the biopsy needle must be inserted through the rectal wall and into the prostate to take tissue samples. This entails an infection risk. In some cases, sepsis may occur. This can lead to permanent residual symptoms and even death in some cases.

29. The risk of infection can be reduced to some extent by the use of antibiotics and by cleaning the bowels, but in recent years there has been an increase in antibiotic-resistant fecal flora, such that antibiotics cannot effectively reduce the risk of infection.

30. A second problem with this technique is that a fairly large number of clinically significant cancers are found at sites of the prostate that are difficult to reach using the transrectal approach[13].

The problems associated with conventional transperineal (TPUS) biopsy procedures

31. In the conventional transperineal (TPUS) technique, tissue is obtained by inserting the biopsy needles through the perineum into the prostate. The risk of infection is lower with this technique, because the needle does not have to pass through the rectum. No antibiotics need to be administered and no bowel preparation is required to reduce the risk of bacterial contamination. In addition, this technique provides a more effective method of accessing the prostate, allowing the target areas of the prostate to be reached that are difficult to reach using the transrectal approach[14].

32. The main disadvantage of the conventional transperineal method is that a biopsy probe must be used for the procedure, and multiple perforations of the perineum must be made (generally between 12 and 55 perforations). Due to the equipment used and the discomfort associated with the procedure, this procedure is generally only suitable for use with a general anesthetic.

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[10] See EP 811, para. [0003].

[11] See EP 811, para. [0004].

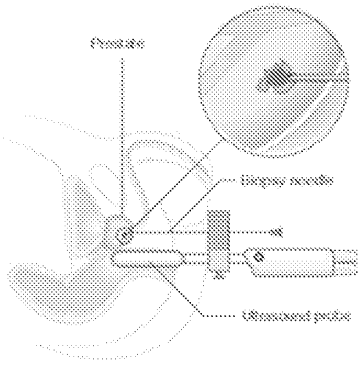
[12] See Dr Popert's expert report (**Exhibit 5**), paras 30 - 39.

[13] See EP 811, para. [0004]; see also Dr Popert's expert report (**Production 5**), para 37.

[14] See EP 811, para. [0005]; see also Dr Popert's expert report (**Production 5**), para 36.

33. Dr. Popert describes the advantages and disadvantages of the conventional transperineal technique in the following terms [15]:

> *"40. As an alternative to the transrectal route, the prostate can be accessed via the perineum. The perineum is the area of skin between the scrotum and the anus. A schematic illustration is shown below, showing how the biopsy needle punctures the skin of the perineum and passes through the tissue behind it to reach the prostate.*

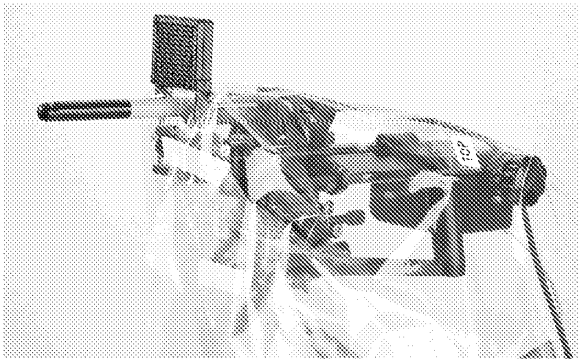


> *41. An advantage of the conventional transperineal technique over the transrectal technique is that the biopsy needle is not required to pass through the non-sterile tissues of the rectum. Consequently, there is no risk of introducing faecal matter into the prostate. The risk and incidence of infections are much lower with the transperineal procedure.*
>
> *42. Another advantage of the transperineal approach is that its different orientation allows access to parts of the prostate (in particular the anterior prostate) that are difficult to reach by the transrectal route.*
>
> *43. The major disadvantage was that the need to make multiple perineal punctures during a template-mapping transperineal biopsy required a general anaesthetic, because of patient discomfort. For each sample taken, the biopsy needle had to be repositioned and a new puncture path through the perineum and intermediate tissue into the prostate had to be made. The original description of transperineal mapping biopsy required one core to be taken for every cubic centimeter of the prostate. A standard prostate volume of 30cc would*

[15] See Dr Popert's expert report (**Exhibit 5**), paras 40 to 49.

require 30 cores, 50cc up to 50 cores, and 100cc up to 100 biopsy cores. Each core taken required a separate puncture of the skin and perineal tissue.

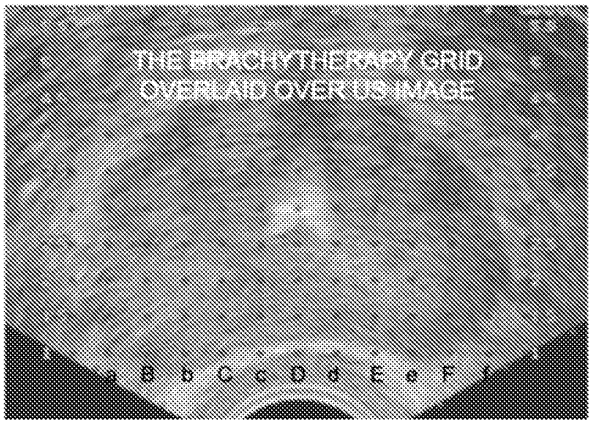
44. To aid the urologist to systematically carry out the multiple perineal puncture biopsies, the standard procedure was to use a brachytherapy grid template to guide the biopsy needle. I have reproduced an example below, showing a grid of 13 x12 positions (making for 156 potential distinct puncture holes). The combination of grid and probe is attached in a fixed position on to a stepper unit which allows the fixed probe to be advanced into the patient's rectum to visualize the prostate by ultrasound and to position the grid against the patient's perineum. The whole system is supported by a stabilization arm, which is fixed to the operating table. The system is complicated to set up, is heavy and cumbersome, and requires cleaning after every procedure. It also requires specialist training to be used properly.



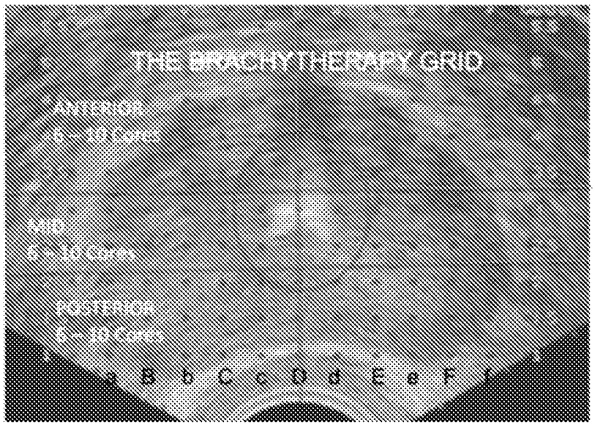
Brachytherapy grid, ultrasound probe fixed to stepping unit and stabilisation arm with sterile drape

45. Once the ultrasound probe has been advanced into the rectum, the prostate is visualized. The brachytherapy grid is advanced so that it rests against the perineum. An image of the brachytherapy grid is overlaid on the ultrasound screen by the ultrasound software. The surgeon uses the apertures of the grid as a needle guide to insert the biopsy needle through the grid apertures which overlay the prostate image, through the superficial perineal skin, the deep perineum and finally into the prostate to sample different areas of the prostate gland, avoiding, if possible, the central region containing the urethra.

46. The images below show that for a normal sized prostate of 30 to 40 cc, it is necessary to take between 36 and 60 samples through multiple separate punctures.



An average sized prostate of 30 - 40 cc



36 – 60 Cores (separate punctures) taken in an average sized prostate

The central urethral area is outlined in red

47. It will be appreciated that this transperineal procedure, while "cleaner" than the transrectal procedure, was much more invasive, and associated with much more discomfort

to the patient, compared to the transrectal route, such that it almost invariably had to be carried out under a general anaesthetic.

48. The equipment in common use for perineal biopsies at the priority date, and the requirement for general anaesthesia, made this a resource-intensive and costly procedure. To conduct a perineal biopsy, an operating theatre, a specialist trained urologist and associated specialist staff, including an anaesthesiologist, would be required.

49. As compared to transrectal biopsy, significantly more hospital time is required per patient with a transperineal approach under general anaesthetic, both during the procedure, as well as post-procedure. Transperineal grid biopsy under general anaesthetic generates waiting lists and leads to delays in diagnosis (and ultimately treatment). Although it is associated with less sepsis than TRUS biopsy, it is recognised that there is a greater risk of other complications, including bleeding, worsening urinary symptoms and retention of urine, which can also result in urinary sepsis".

The device of the invention

34. In contrast to the grid-guided systems of the prior art, the patented device, and in particular the presence of an *access needle* in the device through which the biopsy needle is guided, allows transperineal biopsies to be taken through only two perforations in the perineum, one to the left side and one to the right side of the urethra. Additional perforations in the skin of the patient are not necessary[16].

35. This in turn means that the device of the invention can be used with a local anesthetic, rather than a general anesthetic[17] . As Dr Popert explains, this is a very important advantage for clinical practice, since it means that transperineal biopsies no longer need be performed in the operating theatre, where they are usually carried out, but can be carried out instead in the outpatient setting. This frees up the operating room and the anesthesiologist for other procedures [18]:

"52. Prior to the patent (again, in fact prior to the advent of the PrecisionPoint™ transperineal access system), urologists were thus effectively faced with a choice between transperineal biopsies under general anesthesia or transrectal biopsies under local anesthesia.

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[16] See EP 811, para. [0085]; see also Dr Popert's expert report (**Exhibit 5**), para 55.

[17] See EP 811, para. [0033]; see also Dr Popert's expert report (**Exhibit 5**), para 55.

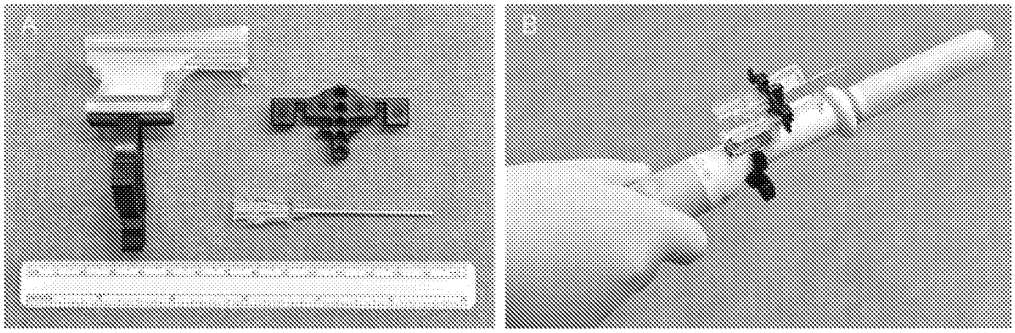
[18] See Dr Popert's expert report (**Exhibit 5**), paras 52 to 59.

53. As will be appreciated from what is set out above, transrectal biopsies had the benefit of being quick and cost-effective, and could be carried in the out-patient setting under local anaesthetic, but they came with a significant and increasingly unacceptable risk of infections and potential missed diagnoses. Transperineal biopsies, on the other hand, had a lower risk of infection, but were more complex to carry out and required general anaesthesia (which in turn meant they had to be carried out in operating theatres).

54. In general, clinicians adopted a policy according to which patients were stratified by risk to one or the other. A policy adopted across our cancer network was that all patients who had a previous negative transrectal biopsy would be offered a transperineal biopsy. All patients being considered for active surveillance were offered a confirmatory transperineal biopsy. Patients at risk of sepsis, diabetics, and the immune-compromised were recommended to have a transperineal biopsy, rather than a TRUS biopsy.

55. In 2016, I was introduced to the PrecisionPoint™ Transperineal Access System, a device that resolves the dilemma facing clinicians. With the PrecisionPoint™ device, it is possible to perform both targeted and systematic transperineal prostate biopsies under local anaesthetic, in an outpatient setting, using only two perineal puncture sites. The device has an innovative design that makes it simple to use, efficient and significantly cheaper than the traditional transperineal equipment. It can be used in conjunction with commonly available handheld rectal transducer probes.

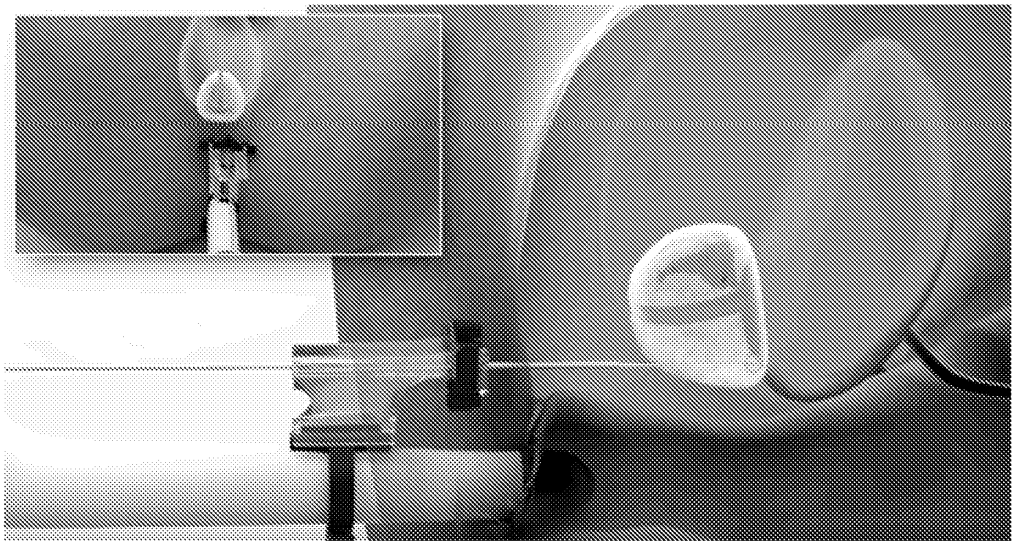
56. I have reproduced an image of the PrecisionPoint™ system, including how it attaches to a held hand transducer, below.



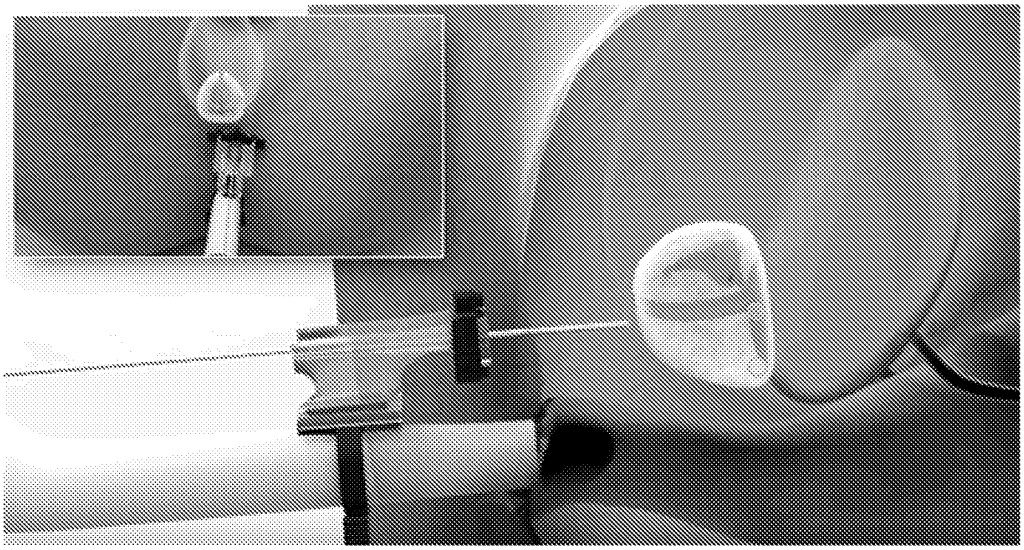
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57. A unique feature of the PrecisionPointTM device is that it uses an access needle intended for the introduction of the biopsy needle. This access needle is the needle shown above.

58. The access needle is first used to guide the local anaesthetic infiltration of the skin and periprostatic tissues. Once anaesthesia has been confirmed, prostate biopsies are taken by advancing the biopsy gun needle through the access needle. Multiple subsequent biopsy cores can then be taken, via the access needle, through the same hole in the perineum. By tilting or angulating the access needle, which is connected to the probe with the attached PrecisionPoint™ device, the clinician can target different sites of the prostate through one and the same perineal puncture point. An explanatory animation video is available on YouTube[19], and I have reproduced two screenshots from the video below.



[19] https://www.youtube.com/watch?v=vV60sUQexuE



59. The ability to take multiple biopsy samples through a single access hole has made it possible to perform perineal biopsies under local anaesthetic in the outpatient setting. Using the PrecisionPoint™ device, it is possible to sample the entire prostate through just two punctures in the perineum: one to the left of the urethra, and one to the right.

60. The procedure is extremely well tolerated by patients and takes a comparable amount of time as a transrectal biopsy. Importantly, it has proved straightforward to teach urologists, specialist urology nurses, radiologists and radiographers how to use the device effectively. The introduction of the PrecisionPointTM Transperineal Access System has revolutionised prostate biopsy procedures within the UK by removing the major barrier that prevented transperineal biopsies from being carried out on a larger scale."

36. These advantages of the invention are also set out in, for example, para. [0085] of the description of EP 811.

<u>The claims of EP 811</u>

37. The invention is claimed in EP 811 as follows:

"*1. An apparatus (100), comprising:*

An upper mount (105) comprising a longitudinal axis;
a first stabilization bar (101) and a second stabilization bar (101) extending from the upper mount (105) along the longitudinal axis of the upper mount (105), the first and second stabilization bars (101) separated by a distance; anda
lower mount (104), the lower mount configured to connect with the upper mount (105) to secure a transrectal probe (103) therebetween, the transrectal probe (103) not being fixed and being freely moveable in operation, the upper mount configured to support an access needle, the access needle configured for perforation of subcutaneous tissue of a perineum at an access site of a target area of a patient during a guided and free-handed transperineal prostate biopsy, the upper mount configured to guide the access needle whereby movement of the access needle is fixed relative to movement of the transrectal probe;
wherein the upper mount further comprises a sliding platform (301) configured to slidably receive the access needle,
wherein the sliding platform (301) is configured to slide from a back to a front of the first and the second stabilization bars (101).

2. The apparatus of claim 1, comprising:
a first fastener (102) and a second fastener (102), the first fastener (102) and the second fastener (102) being configured to connect the lower mount (104) to the upper mount (105).

3. The apparatus of claim 2, the first fastener (102) comprising teeth (202), and the second fastener (102) comprising an aperture (201) defined by the second fastener (102), and a flange (203), the aperture (201) configured to receive the teeth (202), and the flange (203) configured to contact the teeth (202) to securely connect the first fastener (102) to the second fastener (102).

4. The apparatus of claim 1, the sliding platform defining a channel configured to receive the access needle, the channel extending along a longitudinal axis of the sliding platform (301) in a direction parallel to the longitudinal axis of the upper mount (105).

5. The apparatus of claim 1, wherein the sliding platform is pivotably attached to the upper mount whereby the sliding platform is laterally movable or vertically pivotable with respect to a longitudinal axis of the transrectal probe.

6. The apparatus of claim 1, comprising:
a sleeve (2607) the sleeve formed by the upper mount (105) and the lower mount (104), the sleeve (2607) configured to slide over an end of the transrectal probe (103).

7. The apparatus of claim 1, wherein the first and second stabilization bars (101) include grooves configured to allow the sliding platform (301) to slide forward and backward along the first and second stabilization bars (101).

8. The apparatus of claim 7, wherein the grooves are built-in an inner portion of the first and second stabilization bars (101).

9. The apparatus of claim 1, wherein the sliding platform (301) is shorter in length than the first and second stabilization bars (101).

10. The apparatus of claim 1, wherein the first and second stabilization bars (101) extend beyond a front edge of the upper mount (105).

11. The apparatus of claim 1, wherein the first and second stabilization bars (101) include a resistance comprising a strip of material so as to prevent the sliding platform (301) from freely moving on the first and second stabilization bars (101).

12. The apparatus of claim 1, wherein a distal point of the first and second stabilization bars (101) are offset (501) from a fastener (102) configured to connect the lower mount (104) to the upper mount (105).

13. The apparatus of claim 1, wherein the sliding platform (301) is interchangeable from the first and second stabilization bars (101).

14. The apparatus of claim 1, wherein the sliding platform (301) comprises a hole (302) in the center of the sliding platform (302) configured to slidably receive the access needle, the sliding platform being shorter than a distance between the first and second stabilization bars (101, 101) as to accommodate the sliding platform (302) while also securing it to the guide (100)."

15. The apparatus of claim 1, wherein the lower mount (104) is curvilinear and flexible and configured to bend in order to connect the upper mount (105) to secure the transrectal probe (103) therebetween."

38. The Dutch translation of the claims reads as follows:

""1. Inrichting (100) omvattend:
een bovenste steun (105), die een lengteas omvat;
een eerste stabilisatiestang (101) en een tweede stabilisatiestang (101), die zich uitstrekken van de bovenste steun (105) langs de lengteas van de bovenste steun (105), waarbij de eerste en de tweede stabilisatiestang (101) gescheiden zijn door een afstand; en
een onderste steun (104), waarbij de onderste steun is geconfigureerd om met de bovenste steun (105) te worden verbonden om een transrectale sonde (103) daartussen te bevestigen, waarbij de transrectale sonde (103) in werking niet is vastgemaakt en vrijelijk beweegbaar is, waarbij de bovenste steun is geconfigureerd om een toegangsnaald te ondersteunen,
waarbij de toegangsnaald is geconfigureerd om subcutaan weefsel van een perineum te doorboren bij een toegangszijde van een doelgebied van een patiënt tijdens een gestuurde transperineale prostaatbiopsie met vrije hand, waarbij de bovenste steun is geconfigureerd om de toegangsnaald te geleiden, waarbij de beweging van de toegangsnaald gefixeerd is ten opzichte van beweging van de transrectale sonde;
waarbij de bovenste steun verder een glijdend platform (301) omvat, dat is geconfigureerd om de toegangsnaald glijdend op te nemen, waarbij het glijdende platform (301) is geconfigureerd om van een achterkant naar een voorkant van de eerste en tweede stabilisatiestang (101) te glijden.

2. Inrichting volgens conclusie 1, omvattend:
een eerste bevestigingsmiddel (102) en een tweede bevestigingsmiddel (102), waarbij het eerste bevestigingsmiddel (102) en het tweede bevestigingsmiddel (102) zijn geconfigureerd om de onderste steun (104) met de bovenste steun (105) te verbinden.

3. Inrichting volgens conclusie 2, waarbij het eerste bevestigingsmiddel (102) tanden (202) omvat, en het tweede bevestigingsmiddel (102) een opening (201) omvat die is bepaald door het tweede bevestigingsmiddel (102), en een flens (203), waarbij de opening (201) is

geconfigureerd om de tanden (202) op te nemen, en de flens (203) is geconfigureerd om contact te maken met de tanden (202) om het eerste bevestigingsmiddel (102) stevig te verbinden met het tweede bevestigingsmiddel (102).

4. Inrichting volgens conclusie 1, waarbij het glijdend platform een kanaal bepaalt, dat is geconfigureerd om de toegangsnaald op te nemen, waarbij het kanaal zich uitstrekt langs een lengteas van het glijdende platform (301) in een richting evenwijdig aan de lengteas van de bovenste steun (105).

5. Inrichting volgens conclusie 1, waarbij het glijdende platform draaibaar is bevestigd aan de bovenste steun, waarbij het glijdende platform lateraal beweegbaar of verticaal draaibaar is ten opzichte van een lengteas van de transrectale sonde.

6. Inrichting volgens conclusie 1, omvattend:
een huls (2607), waarbij de huls is gevormd door de bovenste steun (105) en de onderste steun (104), waarbij de huls (2607) is geconfigureerd om over een uiteinde van de transrectale sonde (103) te glijden.

7. Inrichting volgens conclusie 1, waarbij de eerste en de tweede stabilisatiestang (101) groeven omvatten, die zijn geconfigureerd om mogelijk te maken, dat het glijdende platform (301) naar voren en naar achteren glijdt langs de eerste en de tweede stabilisatiestang (101).

8. Inrichting volgens conclusie 7, waarbij de groeven zijn ingebouwd in een binnenste gedeelte van de eerste en de tweede stabilisatiestang (101).

9. Inrichting volgens conclusie 1, waarbij het glijdende platform (301) in lengte korter is dan de eerste en de tweede stabilisatiestang (101).

10. Inrichting volgens conclusie 1, waarbij de eerste en tweede stabilisatiestangen (101) zich uitstrekken voorbij een voorste rand van de bovenste steun (105).

11. Inrichting volgens conclusie 1, waarbij de eerste en tweede stabilisatiestangen (101) een weerstand omvatten die een strook materiaal omvat, om te verhinderen dat het glijdende platform (301) vrij beweegt op de eerste en tweede stabilisatiestang (101).

12. Inrichting volgens conclusie 1, waarbij een distale punt van de eerste en de tweede stabilisatiestang (101) verschoven (501) is geplaatst van een bevestigingsmiddel (102), dat is geconfigureerd om de onderste steun (104) te verbinden met de bovenste steun (105).

13. Inrichting volgens conclusie 1, waarbij het glijdende platform (301) van de eerste en tweede stabilisatiestang (101) verwisselbaar is.

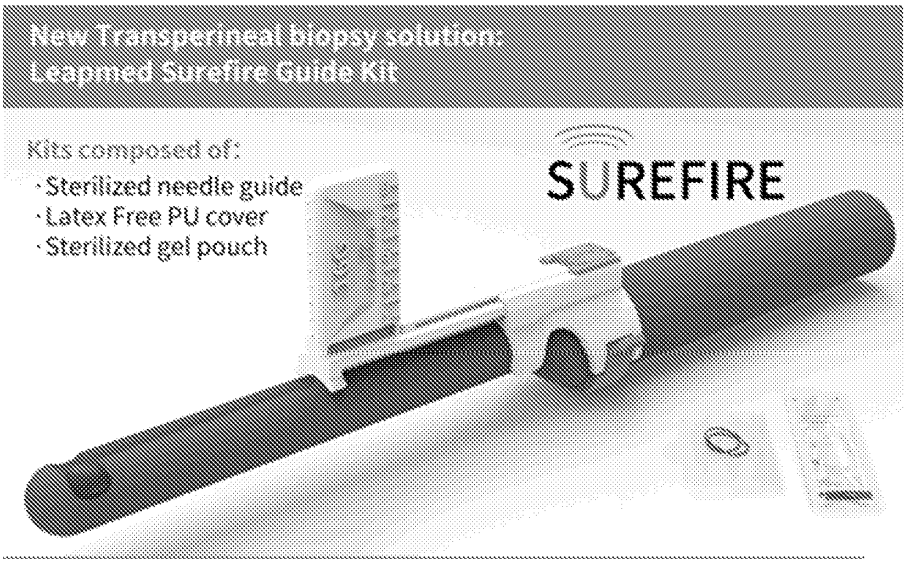
14. Inrichting volgens conclusie 1, waarbij het glijdende platform (301) in het midden van het glijdende platform (302) een gat (302) omvat dat is geconfigureerd om glijdend de toegangsnaald op te nemen, waarbij het glijdende platform korter is dan een afstand tussen de eerste en de tweede stabilisatiestang (101, 101), om het glijdende platform (302) onder te brengen terwijl het ook stevig wordt vastgezet aan de geleider (100).

15. Inrichting volgens conclusie 1, waarbij de onderste steun (104) kromlijnig en flexibel is en is geconfigureerd om te buigen, teneinde de bovenste steun (105) te verbinden om de transrectale sonde (103) daartussen stevig vast te maken".

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The SureFire device

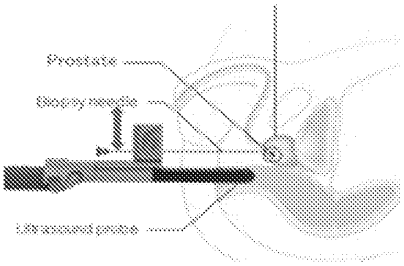
39. In its original form, the SureFire device does not contain an access needle within the meaning of the claims of EP 811. As Mr. Rashid explained in his statement[20], the original SureFire contained a vertical "slice" of a conventional grid, with several recesses through which (and along which) a biopsy needle is inserted to make a multitude of holes in the perineum (much like a conventional grid-guided transperineal biopsy).



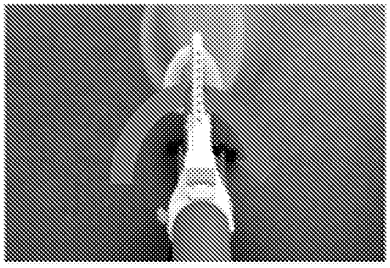
40. So in its original form, the urologist had to make multiple holes in the perineum using the SureFire device, in the conventional way. To reach other parts of the prostate, the urologist had to remove the biopsy needle, turn the grid, and then use the biopsy needle to make new holes in the perineum.

41. This is illustrated in the LeapMed SureFire device instruction manual:

[20] See Mr. Rashid's statement, (**Exhibit 6**), paras 23 - 24.

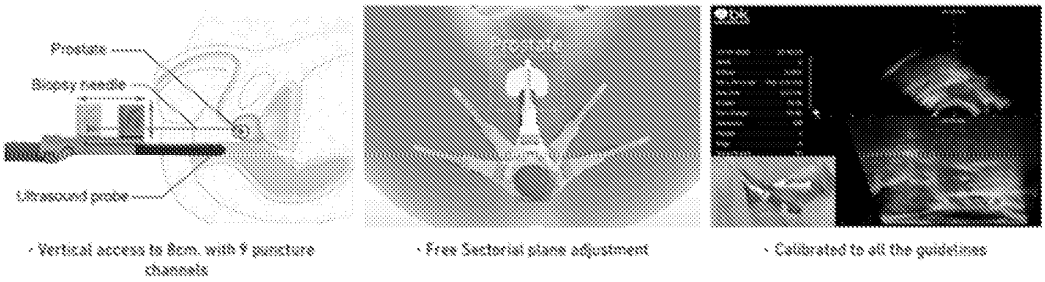


· Vertical adjustable: Up to 9 puncture holes



· Free Sectorial plane adjustment

42. The corresponding section of the US brochure for the LeapMed SureFire device (**Exhibit 8**) is also clear on how the SureFire device should be used:



· Vertical access to 8cm, with 9 puncture channels

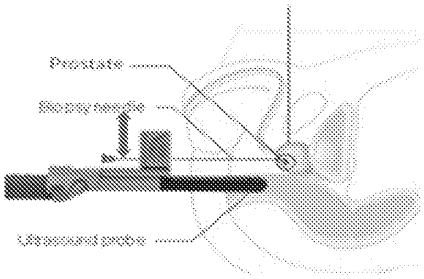
· Free Sectorial plane adjustment

· Calibrated to all the guidelines

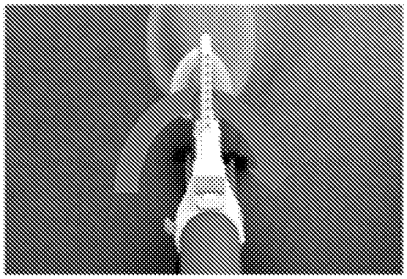
43. However, more recently, the Dutch distributor of the SureFire device, Pelvitec, has taken to providing urologists with a separate instruction sheet with instructions on how to use the Surefire device in conjunction with an access needle. The access needle is not included in the SureFire kit (because the SureFire was not originally intended to be used in this way), but it can be supplied separately by Pelvitec. One of the coaxial access needles recommended by Pelvitec is the Möller Medical 15G x 7.5cm coaxial needle.

44. Mr Rashid discusses the modification in paras 23 to 41 of his statement:

> *"23. The Surefire device was originally intended to be used in a similar way to conventional grid-guided transperineal biopsies. The vertical grey protrusion shown in the image above is in essence a "slice" of the grid typically used to collect biopsy cores in conventional transperineal biopsy procedures by making multiple perforations in the perineum. The biopsy needle is passed through the numbered grooves in order to make multiple perforations and take multiple cores. The device can then be rotated to allow further perforations to be made in other parts of the prostate. This process is illustrated in the brochure as follows:*



·Vertical adjustable: Up to 9 puncture holes



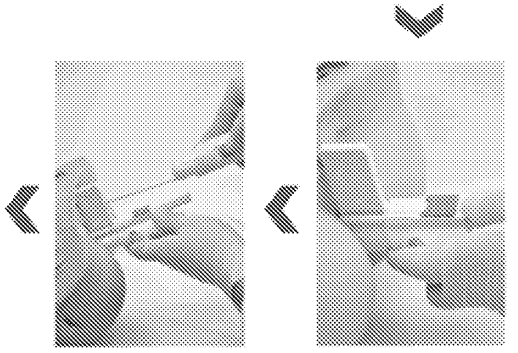
·Free Sectorial plane adjustment

24. As with conventional transperineal biopsy procedures, the making of a significant number of punctures in the perineum will require a general anaesthetic.

25. The modification advocated by the Dutch distributor involves the addition of a coaxial access needle to the Surefire device in one of the grooves of the grey protrusion, through which the biopsy needle can be inserted.

26. The addition of the coaxial access needle allows a biopsy needle to be inserted to take a biopsy sample, with subsequent repositioning of the probe/access needle combination while the access needle remains in place, so that the biopsy needle can then be reinserted, through the same perforation, to take a biopsy from a different area of the prostate. In this way, the number of punctures can be reduced to two, and an intervention is possible under local anaesthetic. This is exactly how the PrecisionPointTM device works.

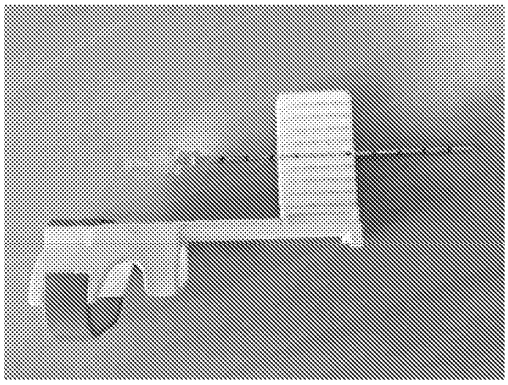
*27. This modification (the addition of an access needle to the Surefire device) is not described in the Surefire brochure, and indeed this way of using the device is not described in the official instructions for use at all. I attach the English-language IFU for the Surefire as **Exhibit SR-2**. They confirm that in normal use, the biopsy needly is simply inserted through the grooves, with the probe being rotated to allow the needle to be inserted at targeted locations:*



6.Rotate the probe to targeted locations. Insert biopsy needle through groove.

5.Unlock/lock button to adjust needle plate to proper position.

*28. The modification (the addition of a coaxial access needle or "coaxial introducer needle") is described in additional information provided by the Dutch distributor, Pelvitec. I attach the instructions provided by Pelvitec to this witness statement as **Exhibit SR-3A** (the Dutch original language version) and **Exhibit SR-3B** (a highlighted version with an English translation of the relevant parts). This document, which bears a footer with Pelvitec's address, shows a photograph of a modified Surefire device with the coaxial access needle in place:*



29. The biopsy needle (not shown in this image) is then passed through the coaxial access needle to take the biopsy cores.

30. The same document explains that the coaxial access need shown in the photograph reproduced above is not present in the packaging for the Leapmed device. That is not surprising, since, as I note above, the use of a coaxial access needle is not contemplated in the instructions for use for the Leapmed device.

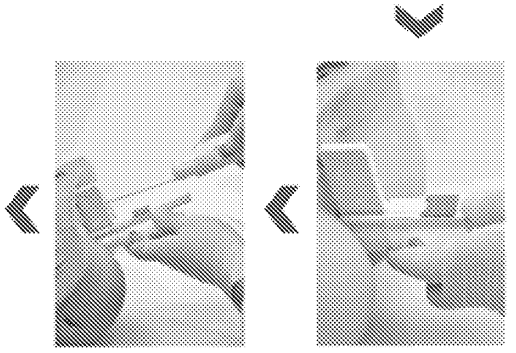
*31. Pelvitec does however supply suitable access needles to allow the modification it advocates to be made. I attach a copy of email correspondence dated 4 June 2021 between a representative of Pelvitec, Mr. Hero Mulder, and a Dutch representative of BXTA, Mr. Wilco van der Lugt as **Exhibit SR-4**.*

32. Although I do not speak Dutch, it has been explained to me, and I believe, that this correspondence relates to the use of coaxial access needles, and that Mr. Mulder confirms, in his email, that the Surefire is almost always used in combination with a coaxial access needle (i.e. in a manner which is not in accordance with the IFU for the Surefire device).

33. Mr. Mulder goes on to state that Pelvitec can supply two different suitable coaxial needles. Mr. Mulder also notes that the Surefire is already used in a number of Dutch hospitals.

*34. This is also the email in which Mr. Mulder provides Pelvitec's own protocol for using the Surefire. (This is **Exhibit SR-3A**, mentioned above). In these instructions, the clinician is instructed to use the same perforation in the skin for the taking of multiple biopsies, and to move the probe in the horizontal plane from left to right, without rotation.*

35. This is a significant deviation from the official instructions for use of the Surefire, which specifically instructs clinicians to rotate the device, the idea being that the vertical grid is thereby moved to the desired position, so that fresh punctures can be made, using the biopsy needle, through the desired groove, at the desired location. Here again is the relevant part of the official IFU, showing the probe being rotated to the targeted locations before the biopsy needle is inserted through the groove:

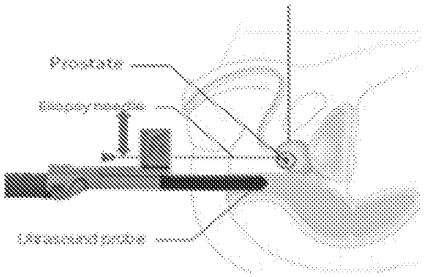


6.Rotate the probe to targeted locations. Insert biopsy needle through groove.

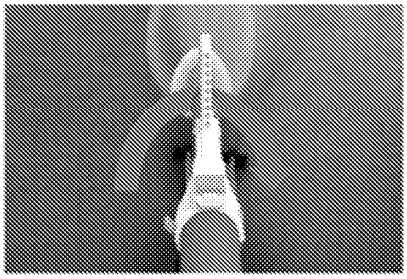
5.Unlock/lock button to adjust needle plate to proper position.

36. The necessity to deviate from the official instructions for use is dictated by the presence of the coaxial access needle, which was not part of the original device or the original IFU, but which is an essential part of the modification proposed by Leapmed and Pelvitec.

37. It is clear that rotating the device in the manner indicated in the official instructions for use while a coaxial access needle is inserted would be impossible without causing trauma. Rotating the coaxial access needle would tear the area around the puncture in which the coaxial needle is embedded. The difficulty can perhaps best be appreciated when considering the following image from the original Surefire brochure:



·Vertical adjustable: Up to 9 puncture holes



·Free Sectorial plane adjustment

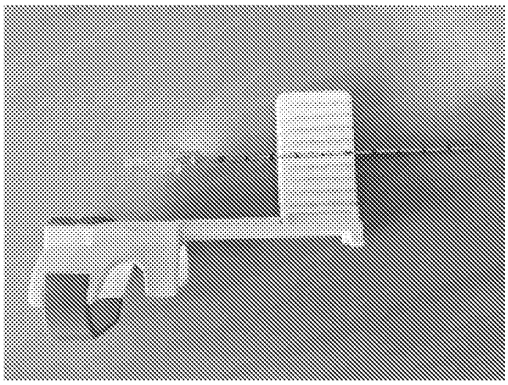
*38. The adaptation of the Surefire device is also illustrated in Leapmed's instruction video. This video, which shows the use of a biopsy needle through the coaxial introducer needle, is exhibited as **Exhibit SR-5**. A number of screen-grabs, accompanied by a transcript of the video, are exhibited as **Exhibit SR-6**.*

39. The addition of the coaxial access needle allows the operator to use the Surefire device in a way it was not intended to be used, in order to obtain the same advantages as those provided by the PrecisionPoint™ device. In effect, the adaptation advocated by Pelvitec turns the Surefire into a poor man's PrecisionPoint™ device, capable of taking multiple biopsies from just two perforations.

40. The modified Surefire device is being targeted by its distributor, Pelvitec, specifically at hospitals in The Netherlands where clinicians have been trained by BXTA and by our regional experts to perform transperineal prostate biopsies under local anaesthetic using the PrecisionPoint™ device.

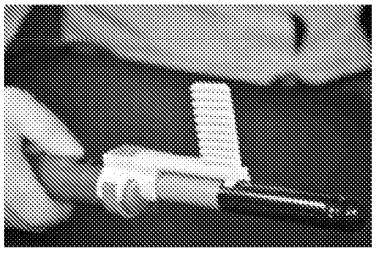
41. In this way, Leapmed and Pelvitec are able to profit from the considerable investments made by BXTA in training clinicians in the use of the PrecisionPoint™ device. Leapmed sells its device at a fraction of the price of the PrecisionPoint™ device. That is no doubt possible because Leapmed did not itself have to make any investments in developing and seeking regulatory approval for the PrecisionPoint™ device, or in training physicians in how the device should be used: it was instead able to benefit directly from the investments Corbin and BXTA had already made."

45. The additional instructions for clinicians provided by Pelvitec (**Exhibit 6/SR-3A**) includes the following photograph showing the SureFire device with an access needle through which the biopsy needle is passed:



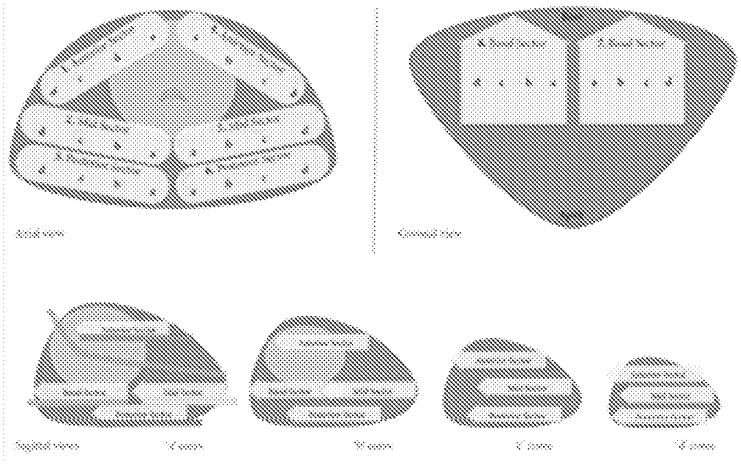
46. The accompanying text makes it clear that the intention is for the biopsy needle to be inserted *through* the same skin perforation *via a coaxial access needle*, and that samples should be taken from only two perforations in the perineum if possible (emphasis added).

> "*Taking biopsies*
>
> *Remove the anesthetic needle and immediately insert the inner coaxial needle and pierce the skin. Preferably at the place where the anesthetic needle went through the skin. Meanwhile keep the probe with the Surefire in the same place.*
>
> *Remove the sharp inner needle from the coax and pass the biopsy needle (preferably a 25 cm needle) through the coax.*
>
> *First biopsies are taken from the target region, after which biopsies are gradually taken from the other regions. If biopsies are taken from a "higher" (more anterior) region, the coaxial needle is placed in a higher conductor but in principle the same skin opening is used.*
>
> *To take several biopsies, move the probe in the horizontal plane from left to right, do not rotate.*
>
> *The Surefire has 9 needle guides*



The lower guides of the Surefire is for biopsying the posterior section.
The two slides above are for the middle section.
To biopsy the anterior section, use the 4th or higher guides.
If possible, the perineal skin is perforated in only 2 places (left/right).

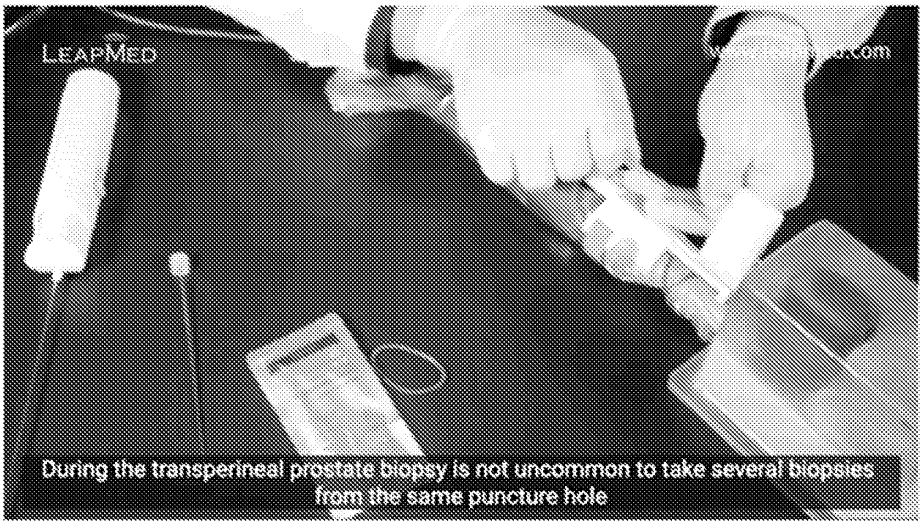
Target biopsies



47. The manufacturers of the device too, LeapMed and AMD, promote the use of the Surefire device with a coaxial introducer needle, and make clear that when such a coaxial introducer needle is used, it is possible *"[...] to take several biopsies from the same puncture hole*". See the screenshots below from LeapMed's Youtube channel[21].

[21] See **Exhibit 8**, a recording of a YouTube video that was available at https://www.youtube.com/watch?v=TxiuS06J2Rs&feature=youtu.be at the time of the preparation of this writ. See also **Exhibit 9** (screenshots of the video).


LEAPMED
Coaxial introducer needle

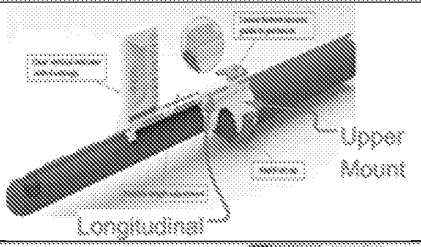
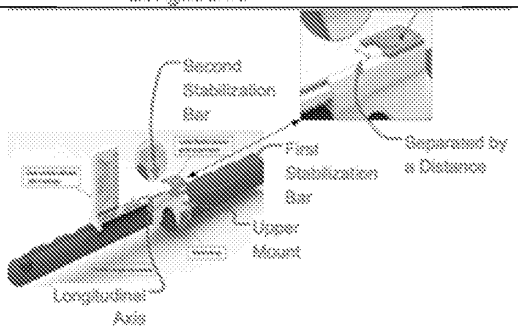
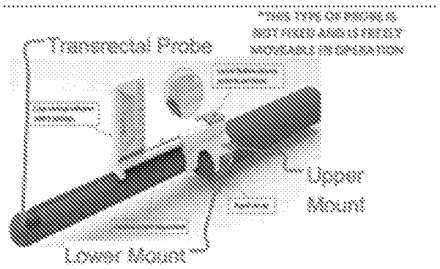
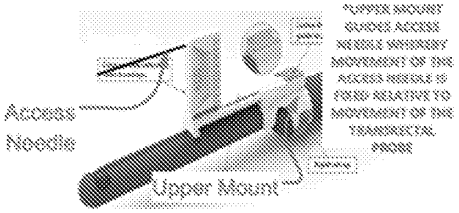


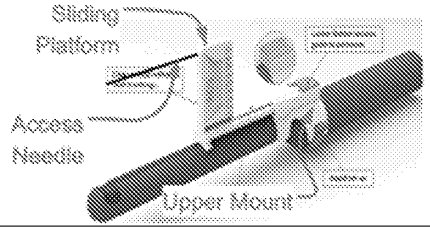
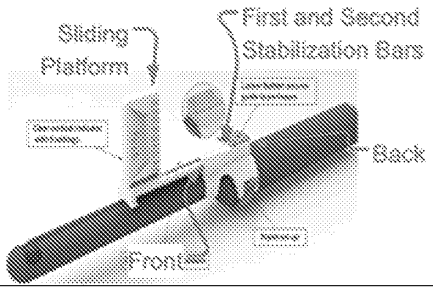
48. The same can be seen in the video on AMD's website (see par. 16above).

Infringement

49. When the SureFire device is fitted with a coaxial needle or access needle[22] in the manner described by Pelvitec (see paras 43- 46above), or LeapMed or AMD, a device emerges which falls within the scope of protection of claim 1 of EP 811:

[22] The access needle is schematically represented below in the mapping of features (iv) and (v) of claim 1. See para. 45 of this writ for Pelvitec's photograph of the actual combination of SureFire + access needle.

	Feature of Conclusion 1	Combination of SureFire with coaxial entry needle
(i)	*An apparatus (100), comprising: an upper mount (105) comprising a longitudinal axis;*	
(ii)	*a first stabilization bar (101) and a second stabilization bar (101) extending from the upper mount (105) along the longitudinal axis of the upper mount (105), the first and second stabilization bars (101) separated by a distance; and*	
(iii)	*a lower mount (104), the lower mount configured to connect with the upper mount (105) to secure a transrectal probe (103) therebetween, the transrectal probe (103) not being fixed and being freely moveable in operation,*	
(iv)	*the upper mount configured to support an access needle, the access needle configured for perforation of subcutaneous tissue of a perineum at an access site of a target area of a patient during a guided and free-handed transperineal prostate biopsy, the upper mount configured to guide the access needle whereby movement of the access needle is fixed relative to movement of the transrectal probe;*	

	Feature of Conclusion 1	Combination of SureFire with coaxial entry needle
(v)	*wherein the upper mount further comprises a sliding platform (301) configured to slidably receive the access needle,*	
(vi)	*wherein the sliding platform (301) is configured to slide from a back to a front of the first and the second stabilization bars (101).*	

50. Pelvitec thus offers for sale and sells, in the course of its business, means relating to an essential element of the invention (the SureFire device and/or the access needles) for the putting into effect of the patented invention in The Netherlands [23], to others than those authorised to work the invention[24]. Pelvitec knows, or it is clear in view of the circumstances, that the means are suitable and intended for the putting into effect of the invention. That constitutes indirect infringement within the meaning of Article 73(1) ROW 1995.

51. To the extent that it might be thought that there would be no *literal* (indirect) infringement (*quod non*), there is in any event (indirect) infringement by equivalence. The modified SureFire device performs essentially the same function as the patented device and operates in essentially the same manner to achieve essentially the same result.

52. It is inconceivable that the European supplier (LeapMed France) or the American supplier (AMD) of the SureFire device is unaware of (or have been unaware of) this practice by their distributor, not least because of the recommendations in the films on their respective websites of YouTube kanalen.

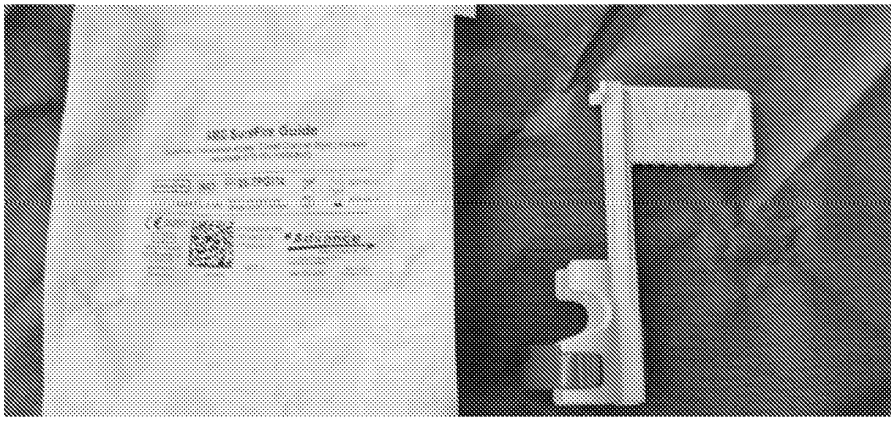
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[23] By making and using a device that falls within the scope of protection of the claims.

[24] That is, to Dutch hospitals, doctors and urologists.

53. The lack of clarity regarding the division of the roles of defendants sub 2 and 3 (LeapMed France and AMD, respectively) has already been discussed in par. 16to 18 above. In brief, according to the European advertising material, LeapMed France is responsible for the distribution of the LeapMed device in Europe. Its name also appears on the IFU (*Instructions For Use*) accompanying the device, which Pelvitec sent to potential Dutch customers at least until a date in September 2021. That LeapMed knew, or at least should have known, about the infringing adaptation of the device is indisputable in view of the LeapMed's video described above.

54. It very recently came to light that defendant sub 3, Advance Medical Designs, also plays a role in the manufacturing and distribution of the SureFire device in Europe. Through a Dutch hospital, Corbin obtained a Surefire device that was sterile packed in packaging on which Advance Medical Designs is mentioned as the manufacturer (see **Exhibit 10** for detailed pictures).



55. In correspondence, Pelvitec has indicated that it obtains its products via Advance Medical Design (**Exhibit 11**). The same was confirmed by Mr Eelbode (**Exhibit 12**).

56. However, this does not mean that LeapMed is out of the picture: the device still bears the name LeapMed. LeapMed France has not responded to the letter of summons; and its name is still listed on the IFU distributed by Pelvitec (as late as September 2021(!)) as the manufacturer's Authorised European Representative.

57. Both AMD and LeapMed France are therefore also directly involved (or have been until recently involved) in the same indirect infringement as their distributor Pelvitec. They too have, in or for their business, offered and supplied means relating to an essential element of the invention (the Surefire device and/or the access needles), for the putting into effect of the patented invention in the Netherlands, to others than those authorized to work the invention.

58. Moreover, each of Leapmed, AMD and Pelvitec induce third parties to infringe and they profit from that infringement. This is tortious under Dutch law.

The fact that the Surefire device can (also) be used in a non-infringing way should not be an obstacle to the requested provisions

59. Corbin does not deny that the use of the Surefire device in its original configuration (i.e. without the currently recommended addition of a coaxial entry needle) will not necessarily give rise to patent infringement.

60. However, in cases where a particular product can be used in both a non-infringing and an infringing manner, it is up to the alleged infringer to ensure that everything is done in its power to prevent infringement at a later stage: Court of Appeal of The Hague, 27 January 2015 (*Novartis v Sun*) ECLI:NL:GHDHA:2015:1769; see also the Supreme Court in its judgment dated 14 April 2017 ECLI:NL:GHDHA:2015:1769.

61. In the present case, Pelvitec, Leapmed and AMD do the opposite. In their instructions to end users, they encourage an infringing modification that is not even consistent with the SureFire device's official instructions for use. In doing so, they have created a market for a low-cost, inferior and infringing variant of the PrecisionPoint™.

62. Pelvitec also deliberately set its sights on hospitals that had already received training in the use of the PrecisionPoint™ Transperineal Access System, so that Pelvitec can benefit from the experience that urologists have gained from using the PrecisionPoint™ device.

63. This has led to disastrous consequences for the Dutch business of the exclusive European distributor of the patented PrecisionPoint™ device (BXTA). Reference is made to the statements of Mr. Rashid and Mr. Van der Lugt of BXTA (**Exhibits 6** and **7**).

64. Given the recent promotion and encouragement by Pelvitec, Leapmed and AMD of (exclusively) the infringing use of their device, it will most likely prove impossible to put the genie back in the bottle by (for example) informing users that they should *not* use the SureFire device with a coaxial access needle. For this reason, a recall order and a ban on all future sales of the SureFire is appropriate.

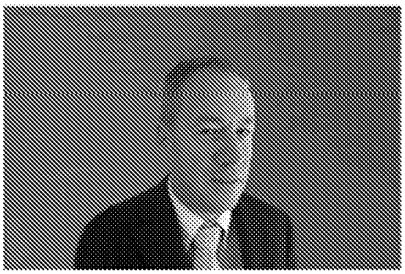
    See - for an example of a case in which the District Court ruled that a warning to users not to use a device (there: a fall protection system) in a certain (infringing) manner was not effective to prevent indirect infringement - the judgment of the District Court of The Hague of 18 October 2010, KG ZA 10-1120 (*Safeway GmbH / Kedge Holding B.V.*). In that case the District Court considered that it was unlikely that a warning would be effective to prevent infringement, not least because the infringer had previously pointed out to users that the device should be used in a way that actually infringes the patent. So too here.

65. Corbin therefore seeks an injunction to recall infringing devices sold by Pelvitec and/or LeapMed France and/or AMD and an order for rectification. A ban for the future and a recall and rectification for the past are the only ways properly to restore the *status quo ante bellum*.

66. Corbin is also seeking a preliminary injunction for the duration of the present proceedings from the date of the virtual hearing until judgment is rendered. Corbin has a legitimate interest in such an injunction because neither Pelvitec nor AMD have expressed their willingness to cease sales in anticipation of the outcome of these proceedings.

Art 843a Rv exhibitor's claim against Nico Eelbode

67. Corbin's lawyers came across Nico Eelbode through a Google search for a contact person for Leapmed France. According to his LinkedIn profile, Mr. Eelbode is a "Consultant" at Leapmed France (**Exhibit 13**). On LeapMed's own website, he is (still) described, on the "*Founders*" page, as "*GM of LeapMed France*" (**Exhibit 14**):



Nico Eelbode

GM OF LEAPMED FRANCE

68. Corbin's lawyers have written to Mr Eelbode, via his LeapMed email address, requesting that the summons letter (**Exhibit 13**) be brought to LeapMed's attention. The correspondence is being brought into the proceedings as **Exhibit 14**.

69. In response to the request, Mr Eelbode stated that he was no longer involved with LeapMed: his cooperation with LeapMed had ended some time ago.

70. However, that statement was impossible to reconcile with the fact that he still had access to a LeapMed email address (eelbode@leapmed.fr)[25] and that he still signs his emails – including, incidentally, the email in which he denied having anything to do with LeapMed – with the signature "*Global Urology BDM Leapmed Healthcare*". "BDM" stands for "*Business Development Manager*". So Mr. Eelbode is apparently still intimately involved in LeapMed's global urology business.

71. When asked to explain these discrepancies, Mr Eelbode had no answer – or at least no coherent answer.

72. He did, however, know that Corbin should be targeting AMD (and in any event not LeapMed France). From a telephone conversation with him it subsequently appeared that AMD was already aware of the summons letter and Corbin's statements – because Mr Eelbode himself had informed AMD of them. He expected AMD to contact Corbin's lawyers immediately[26]. AMD did not do so.

73. Mr Eelbode currently denies involvement in the trade of the SureFire device. Corbin has good reason to doubt the accuracy of this assertion, not least:

    a. because Mr Eelbode provided demonstrably false information regarding his own involvement with LeapMed;

    b. because Mr Eelbode immediately informed AMD of Corbin's claims. That is not the action of someone who has nothing to do with the trade in SureFire devices;

    c. because Mr Eelbode undertook to send the CE dossier and the IFU of the SureFire device to Corbin's lawyers[27]. Someone who was not involved in the trade in SureFire devices would not have such documentation in his possession.

74. Mr Eelbode is therfore apparently still involved (or was involved until very recently) in the trade in the SureFire device. Even if that is not (or no longer) the case, he still possesses relevant information regarding the trading thereof by LeapMed France and/or Advance Medical Designs that will be relevant in tracing the trading channels of the other defendants and of other parties (including also Mr. Eelbode's own companies) that are not yet on Corbin's radar screen.

75. Corbin has a legitimate interest in obtaining copies and/or inspection of documents held by Mr. Eelbode that are relevant to the assessment of patent infringement by Leapmed, AMD and

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[25] After all, he had responded to an email to this email address(!)

[26] Pelvitec thought so too.

[27] He did not send the CE file - he sent another certificate from AMD. Mr Eelbode withdrew his commitment to send the IFU, stating that he would not have the document anyway.

Pelvitec and by Mr. Eelbode himself or by his own companies. Corbin seeks copies of the following information:

- All (email) correspondence between Mr. Eelbode and LeapMed and/or AMD regarding the SureFire device, complete with attachments;
- All other documentation pertaining to the SureFire device, including purchase and sales documentation, import and export documentation, (email) correspondence with customers, orders, pre-orders and invoices; and
- All documentation showing which parties are involved in the manufacturing, import and trading of the SureFire device as it is marketed in the Netherlands.

Jurisdiction

With regard to Pelvitec B.V.

76. Pelvitec B.V. has its registered office in Delft. The Dutch court has absolute jurisdiction on the basis of Art. 4 Brussels I bis Regulation. As far as the claims for patent infringement are concerned, the District Court of The Hague has exclusive jurisdiction: Art. 80 ROW 1995.

77. The District Court of The Hague also has jurisdiction over the claim in tort. The claim in tort is closely intertwined with the claims in patent law, so that it is necessary to handle the claims together. Furthermore Pelvitec has its registered office in Delft, within the district of the District Court of The Hague.

With regard to LeapMed France

78. The District Court of The Hague has jurisdiction under Art. 7(2) Brussels I bis-Vo against LeapMed France. That entity is also committing indirect infringement in the Netherlands by supplying SureFire devices to Pelvitec for further sale in the Netherlands, with the intention that they will be adapted by the end user to apply the invention. These infringing acts will qualify as unlawful act, whereby the harmful event will occur in The Netherlands, among other countries. In addition, the Hague Court also has jurisdiction against LeapMed France based on article 8(1) Brussels I bis Regulation and article 35 Brussels I bis Regulation.

Concerning the American defendant Advance Medical Designs

79. Pursuant to art. 6 sub e Rv the District Court of The Hague has jurisdiction against AMD. That entity is also committing indirect infringement in the Netherlands by supplying SureFire devices to Pelvitec for further sale in the Netherlands, with the intention that these will be adapted by the end user to put into effect the invention. These infringing acts also qualify as unlawful act, whereby the harmful event will occur in the Netherlands, among other countries. In addition, the District Court of The Hague has jurisdiction against AMD based on art. 7(1) Rv and art. 13 Rv.

In respect of the natural person Nico Eelbode

80. The District Court of The Hague also has jurisdiction to hear the claim against Mr Eelbode, based on Art. 8(1) Brussels I bis Regulation and Art. 35 Brussels I bis Regulation.

81. The judge in preliminary relief proceedings of the District Court of The Hague has relative jurisdiction on the basis of Article 80 (2) (c) ROW, which came into force on 1 August 2021.

Known Defences of the Defendants

82. In correspondence prior to this litigation, Pelvitec took the position that there had been a number of infringement cases in the U.S. between Corbin and Pelvitec's supplier AMD, all of which Corbin had lost.

83. This statement is factually incorrect.

84. Pelvitec has also claimed that AMD has initiated an "*anti-harrassment*" suit against Corbin in the U.S.. This claim is also factually incorrect (or at least Corbin is not aware of such a lawsuit). The statement is also irrelevant to the issue of patent infringement by Pelvitec and AMD.

85. AMD itself has not responded substantively to Corbin's summons.

86. Mr Eelbode has said that he has no information other than that already sent (i.e. the wrong CE certificate). This is not credible for the reasons outlined above.

87. LeapMed France did not respond at all to Corbin's summonses (except indirectly, through Mr Eelbode).

88. Corbin is not aware of any other defenses that Defendants may raise.

Proof

89. Corbin refers to the exhibits mentioned in this writ, and to possible additional exhibits which will be submitted before the virtual hearing in summary proceedings.

WHEREFORE:

May it please the Interim Injunction Judge of the District Court of The Hague, in a judgment which is provisionally enforceable:

Provisional

I. to prohibit Pelvitec BV, Leapmed France SAS and Advance Medical Designs Inc, with immediate effect after service of the provisional judgment to be rendered at the virtual

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hearing, until judgment is delivered in the main action in these proceedings for interim relief from directly or indirectly infringing the Dutch part of the European patent EP 3 125 811 B1, including by offering or supplying to third parties, in or for their business, an essential element of the invention embodied in EP 3 125 811 B1 for the application of the patented invention and/or act unlawfully (in any other manner) towards Corbin, including by directly or indirectly promoting, facilitating, participating in and/or profiting from an infringement of European Patent EP 3 125 811 B1;

In the main proceedings in these proceedings for interim relief

II. to prohibit Leapmed France SAS, Advance Medical Designs Inc and Pelvitec B.V., with immediate effect after service of the judgment to be rendered in this matter, from the direct or indirect infringement of the Dutch part of the European patent EP 3 125 811 B1, including by offering or supplying to third parties, in or for their business, an essential element of the invention embodied in EP 3 125 811 B1 for the application of the patented invention and/or act unlawfully (in any other manner) towards Corbin, including by directly or indirectly promoting, facilitating, participating in and/or profiting from an infringement of the European patent EP 3 125 811 B1

III. to order Leapmed France SAS, Advance Medical Designs Inc and Pelvitec B.V. to provide Corbin's lawyer with a list of the names of all customers, partners, service providers or other third parties to whom Leapmed France SAS, Advance Medical Designs Inc and Pelvitec B.V. have sold and/or offered the SureFire products, substantiated by all relevant purchase and sales documentation, including but not limited to readable emails, order confirmations, invoices and copies of other incoming and outgoing documents. have sold, supplied and/or offered the SureFire products, supported by all relevant purchase and sales documentation, including but not limited to legible emails, orders, order confirmations, invoices and copies of other purchase and sales documents, including all leaflets and annexes or attachments to emails or other purchase or sales documents describing how the SureFire device is to be used;

IV. to order Pelvitec B.V. to send, within 2 (two) days of service of the judgment to be rendered, a letter of rectification on its usual letterhead and in its usual typeface, signed by a person authorized by statute, to all of its purchasers, and to send a copy of each letter of rectification with proof of mailing simultaneously and without further comment to plaintiffs' counsel, stating

[Date]
Dear [name of addressee],

RECTIFICATION

The Interim Injunction Judge of the District Court of The Hague ordered us by judgment dated [date of judgment] to make the following statement:

In the district court's preliminary opinion, we infringed the Dutch portion of European patent EP 3 125 811 B1, held by Corbin Clinical Resources LLC, by supplying our Surefire device along with instructions advising its use with a coaxial access needle.

The court ordered us to immediately cease and desist all infringement of this patent. The court also ordered us to recall the infringing Surefire devices, refund the purchase price, and reimburse us for transportation costs.

Please return any remaining Surefire devices that you have in stock. We will refund the purchase price and transportation costs.

Kind regards,

[defendant's name]

_____ *[signature]*

or a message to be determined by the judge in good justice;

V. to order Pelvitec B.V., within one (1) day after service of the judgment to be rendered in this case, to post and maintain on the homepage of its website(s) the following message, clearly and immediately visible and legible, in all languages in which the website is available, and without further comment:

RECTIFICATION

The Interim Injunction Judge of the District Court of The Hague ordered us by judgment dated [date of judgment] to make the following statement:

In the district court's preliminary opinion, we infringed the Dutch portion of European patent EP 3 125 811 B1, held by Corbin Clinical Resources LLC, by supplying our Surefire device along with instructions advising its use with a coaxial access needle.

The court ordered us to immediately cease and desist from all infringement of the patent. The court also ordered us to recall the infringing products, refund the purchase price, and reimburse transportation costs.

We have requested our customers to return the infringing products sold or supplied by us.

Kind regards,

or a message to be determined by the judge in good justice;

Regarding Nico Eelbode

VI. to order Mr. Eelbode on the basis of art. 843a Rv to provide Corbin, within 7 (seven) days after service of the court order, with copies of all documents in his possession, in any capacity whatsoever, pertaining to the Surefire device, including (but not limited to) all (email) correspondence between Mr. Eelbode and/or LeapMed and/or AMD pertaining to the SureFire device, complete with attachments; all other documentation pertaining to the SureFire device, including purchase and sales documentation, import and export documentation, (email) correspondence with customers and/or suppliers, orders, pre-orders and invoices; and all documentation showing which parties are involved in the manufacturing, import and trade of the SureFire device as marketed in the Netherlands, all under penalty of an immediately payable penalty of EUR 50.000 (in words: fifty thousand Euro) for each day, whereby part of a day counts as a full day, that Mr Eelbode does not comply or does not comply fully and on time with this order, with a maximum of EUR 1,000,000 (in words: one million Euro) in penalty payments to be forfeited;

In both the provisional application and the main proceedings

VII. to order that LeapMed France SAS, Advance Medical Designs Inc. and Pelvitec B.V. for each violation of the preliminary injunction as described under (I) or of the injunction in the main action as described under (II) and/or each failure to (fully or timely) comply with the injunctions mentioned under (III) through (V) each forfeit a penalty payment of EUR 500,000 or, at the discretion of Corbin, that Leapmed France SAS, Advance Medical Designs Inc. and Pelvitec B.V. each forfeit a penalty payment of EUR 10,000 (in words: ten thousand Euros) for each SureFire product with which they infringe directly or indirectly, or by which they act unlawfully or, at the discretion of Corbin, that Leapmed France SAS, Advance Medical Designs Inc. and Pelvitec B.V. each forfeit a penalty payment of EUR 100.000 (in words: one hundred thousand Euros) for each day, whereby part of a day counts as a full day, that Leapmed France SAS, Advance Medical Designs Inc. and Pelvitec B.V. do not fully and timely comply with the orders referred to under (III) through (V);

VIII. to order LeapMed France SAS, Advance Medical Designs Inc. and Pelvitec B.V. jointly and severally to pay Corbin's reasonable and proportionate costs of the proceedings within the

meaning of Art. 1019h Rv;

IX. to order Mr Eelbode to pay the legal costs of Corbin according to the court-approved scale of costs in the specific disclosure application against him pursuant to Art. 843a Rv;

X. to declare that the judgments to be given in this case are provisionally enforceable.

The cost of this writ is:

This case is handled for the **plaintiff CORBIN** by Simon Dack (simon.dack@hoyngrokh.com, tel: 06 319 419 07) and Peter van Schijndel (peter.vanschijndel@hoyngrokh.com), tel: 06 509 793 97), HOYNG ROKH MONEGIER B.V., tel: 020 592 4423, fax: 020 463 7296.

Defendants PELVITEC and **AMD** are assisted by Jaap Bremer (jaap.bremer@barentskrans.com, tel. 070 376 06 25).

Defendant NICO EELBODE can be reached at: eelbode@leapmed.fr, tel: + 33 6 767 560 96.

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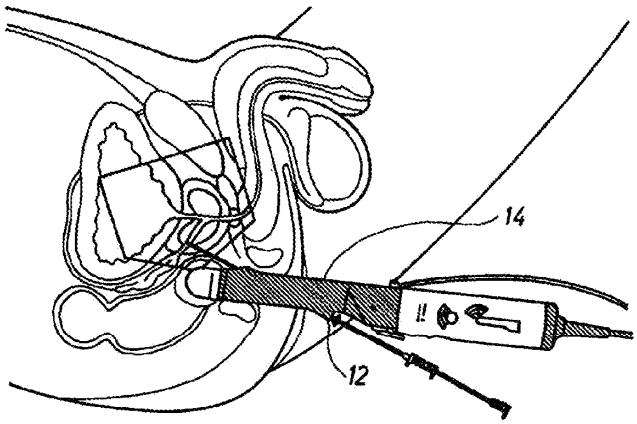
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With amended claims.

(54) Title: ULTRASOUND PROBE WITH A DETACHABLE NEEDLE GUIDE, FOR COLLECTING TISSUE SAMPLES



(57) Abstract

An apparatus for insertion into the human body and which comprises one or more optionally scanning transducers (17, 18) and a needle guide (12), which can be operated from the outside. The needle guide (12) is used for collecting tissue samples from the human body. According to the invention the needle guide (12) is separated from the other part of the apparatus which for hygienic reasons is covered by a sterile sheath (14). The needle guide (12) is thus attached to the other part of the catheter via the sheath. In other words the needle guide (12) is arranged outside the sheath (14) in such a manner that the needle not penetrate the sterile sheath (14), which otherwise would entail that the apparatus should be disinfected after use.

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ULTRASOUND PROBE WITH A DETACHABLE NEEDLE GUIDE, FOR COLLECTING TISSUE SAMPLES

Technical Field

The invention relates to an apparatus for insertion into the human body and which comprises one or more optionally scanning transducers of which at least one preferably scans in the longitudinal direction, and a needle guide, which can be operated from the outside and used for collecting tissue samples from the human body.

Background Art

When inserted into a patient's anus, such an apparatus is able to locate the internal organs, such as the prostate. If a sample is to be obtained from the area adjacent the neck of the bladder, it is possible to collect the sample by inserting a needle from the outside, the needle holder being attached to the apparatus as shown in Fig. 1. However this requires that a local anaesthetic is applied to the insertion point of the needle, as the area close to the surface of the skin contains many sensory nerves. It is however desirable to avoid such a local anaesthetic. Accordingly it has been desired to insert the needle through the intestinal wall at the anus, confer Fig. 2, whereby a local anaesthetic is not required, as the internal organs are not that sensitive. At the same time it is desirable that the apparatus is covered by a sterile sheath in use such that subsequent disinfection thereof is avoided, naturally the sterile sheath must not be damaged by the needle guide.

Brief Description of the Invention

The object of the invention is thus to provide an apparatus with a needle guide which cannot damage a sterile sheath. At the same time the needle is to be in a plane substantially in the longitudinal direction.

An apparatus of the above type is according to the invention characterised in that the needle guide is separate from the other part of the apparatus which for hygienic reasons is covered by a sterile sheath. The needle guide is thus attached to the part of the apparatus on the outer side of the sterile sheath. In other words the needle guide is arranged outside the sheath such that the needle need not penetrate the sheath, which otherwise would entail that the apparatus should be disinfected after use.

In a particularly advantageous embodiment of the invention the needle guide is retained by being pressed into a recess in the other part of the apparatus after the sterile sheath has been placed on the apparatus. The needle guide is typically disposable and can be discarded after use.

Optionally according to the invention the needle guide may be retained by means of a needle guide holder which is clipped firmly onto the other part of the apparatus after the sterile sheath has been arranged on the apparatus.

Brief Description of the Drawings

The invention is explained in greater detail below with reference to the accompanying drawings, in which

Fig. 1 shows a known apparatus for insertion into the human body,

Fig. 2 shows an apparatus according to the invention for insertion into the human body, and

Figs. 3 and 4 show an optional embodiment of the apparatus according to the invention in assembled and separated state.

Best Mode for Carrying Out the Invention

Transrectal ultrasound scanning of the prostate is a valuable method for detection and monitoring of diseases in the prostate.

Fig. 1 shows a known apparatus 1 for insertion into a patient's anus. By means of the apparatus an ultrasound scanning of for instance the prostate can be performed. Based on the ultrasound image of the prostate, a biopsy stylet is then inserted, a special holding member 2 for the stylet being attached to the apparatus. The holding member 2 ensures that the stylet is inserted substantially parallel to the apparatus 1. The holding member 2 is provided with a plurality of holes such that the suitable distance to the apparatus can be selected. During insertion, the stylet is visible on the ultrasound image. However it may be necessary to apply a local anaesthetic before inserting the stylet.

Fig. 2 shown an apparatus according to the invention for insertion into the human body through the intestinal wall near the anus. At the end of the apparatus two ultrasonic transducers 17, 18 are provided; one ultrasonic transducer 17, which is able to scan in the longitudinal direction of the apparatus, and one ultrasonic transducer 18 which is able to scan across the longitudinal direction. As a result a fine image of the positioning of the patient's internal organs is obtained. It may be of interest to have a screen display of the precise position of the prostate.

The apparatus with the ultrasonic transducers 17, 18 is covered by a sterile sheath 14 such that the apparatus never comes into direct contact with the patient, whereby disinfection of the apparatus after use is not needed, as the apparatus is ready for reuse after a minor cleaning thereof when the sheath 14 has been removed. An inclining groove or recess is, however, provided on one side of the apparatus to receive a needle guide 12, after the sterile sheath 14 has been placed on the apparatus. Consequently, the needle guide 12 does not come into direct contact with the apparatus. The

needle guide 12 is, however, retained in relation to the apparatus inter alia due to the additional friction caused by the sheath 14, said friction possibly being provided by means of indentations or grooves. Arranging the needle guide 12 in this manner is particularly advantageous in that the needle thus never penetrates the sheath 14. As a result the apparatus is not unnecessarily contaminated and thus need not be disinfected after each use.

After the apparatus with the needle guide 12 has been inserted into the anus and the internal organs in question have been located on the screen by means of the ultrasonic transducers 17,18, a biopsy needle is inserted through the needle guide 12 and the penetration of the needle, until the needle tip reaches the organ, from which the sample is to be collected, is monitored on the screen.The biopsy needle is inserted through the needle guide 12 by hand.

When the desired number of samples has been collected, the needle and the entire apparatus are removed, whereafter it is sufficient to remove the needle guide 12 and the sheath 14 and clean the apparatus, which then is ready to be reused.

The ultrasonic transducers 17, 18 and the pertaining displays and electronic circuits are conventional types and are thus not described in detail.

Figs. 3 and 4 shows an optional embodiment of the apparatus, in which the needle guide 12 is retained by means of a separate needle guide holder 16. The needle guide holder is clipped firmly onto the other part of the catheter after the sterile sheath 14 has been arranged thereon and is formed of an oblong body of a material, which can be sterilised, such as stainless steel. The oblong body is formed as a sector of a circle in cross-section and substantially fits into a corresponding tap in the other part of the apparatus. The oblong body is provided with a projecting knot 19 mating with a corresponding opening 20 in the tap. When inserted into the opening 20, the needle guide holder is retained by being clipped thereon by means of special clipping mem-

bers led partly around the apparatus. A groove 22, in which the needle guide 12 can be placed, is provided on the plane inner surface of the needle guide holder 16. The needle guide 12 is discarded after use, while the needle guide holder 16 may be disinfected by means of an autoclave.

In an optional embodiment the needle guide and the needle guide holder are formed integrally.

Claims

1. Apparatus for insertion into the human body and which comprises one or more optionally scanning ultrasonic transducers (17,18), of which at least one preferably scanning in the longitudinal direction, and a needle guide (12) which can be operated from the outside and used for collecting tissue samples from the human body, the needle guide (12) being separate from the other part of the apparatus which for hygienic reasons is covered by a sterile sheath (14).

2. Apparatus according to claim 1, characterised in that the needle guide (12) is retained by being pressed into a recess in the other part of the apparatus after the sterile sheath (14) has been arranged on the apparatus.

3. Apparatus according to claim 1, characterised in that the needle guide (12) is retained by means of a needle guide holder (16) which can be clipped firmly onto the other part of the apparatus after the sheath (14) has been arranged on the apparatus.

4. Apparatus according to claim 3, characterised in that the needle guide holder (16) is formed as a sector of circle in cross-section.

5. Apparatus according to claims 3 or 4, characterised in that the needle guide and the needle guide holder are formed integrally.

AMENDED CLAIMS

[received by the International Bureau on 04 June 1999 (04.06.99);
original claims 1-5 replaced by amended claims 1-4 (1 page)]

1. Apparatus for insertion into the human body and which comprises one or more optionally scanning ultrasonic transducers (17, 18), of which at least one preferably scanning in the longitudinal direction, and a needle guide (12) which can be operated from the outside and used for collecting tissue samples from the human body, the needle guide (12) being separate from the other part of the apparatus which for hygienic reasons is covered by a sterile sheath (14), c h a r a c t e r i s e d in that the needle guide (12) is retained by being pressed into a recess in the other part of the apparatus after the sterile sheath (14) has been arranged on the apparatus.

2. Apparatus according to claim 1, c h a r a c t e r i s e d in that the needle guide (12) is retained by means of a needle guide holder (16) which can be clipped firmly onto the other part of the apparatus after the sheath (14) has been arranged on the apparatus.

3. Apparatus according to claim 3, c h a r a c t e r i s e d in that the needle guide holder (16) is formed as a sector of circle in cross-section.

4. Apparatus according to claims 3 or 4, c h a r a c t e r i s e d in that the needle guide and the needle guide holder are formed integrally.

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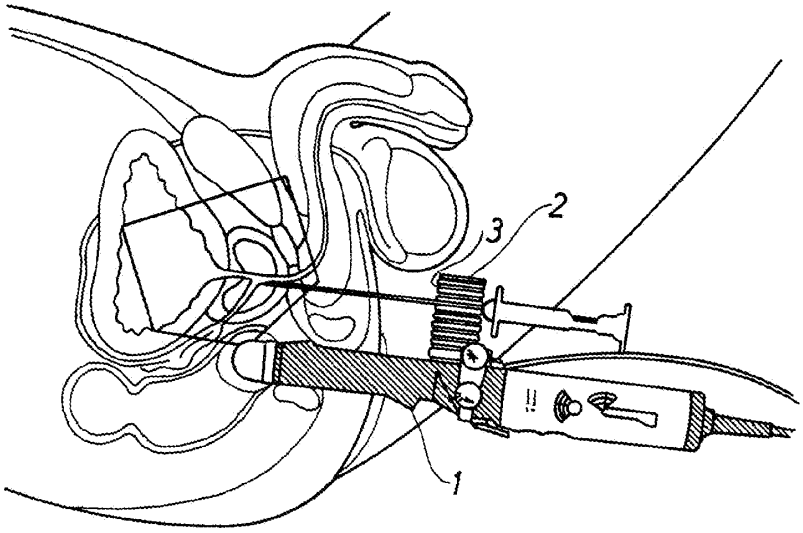


Fig. 1

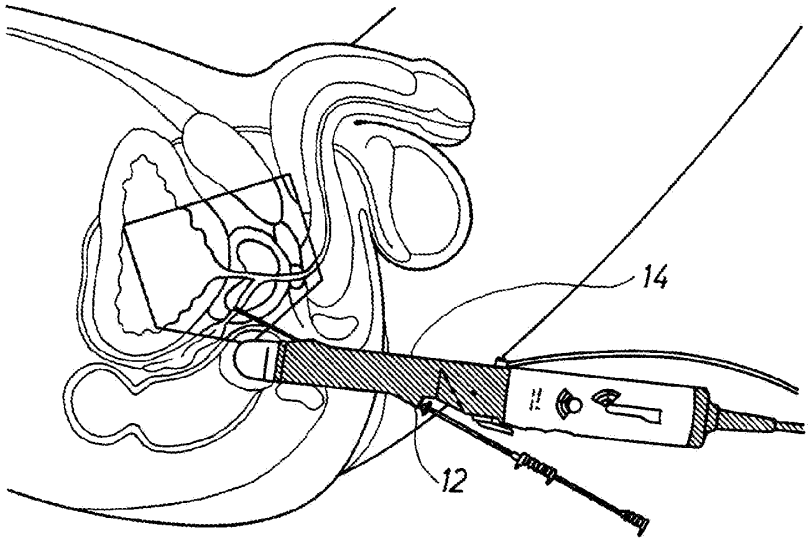


Fig. 2

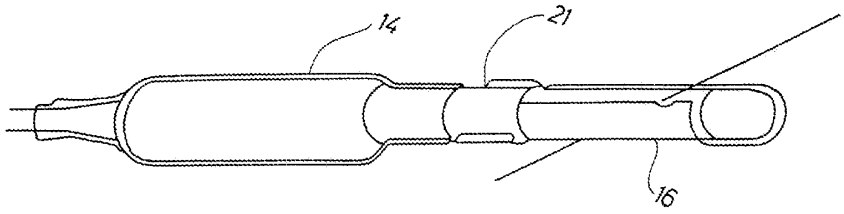


Fig. 3

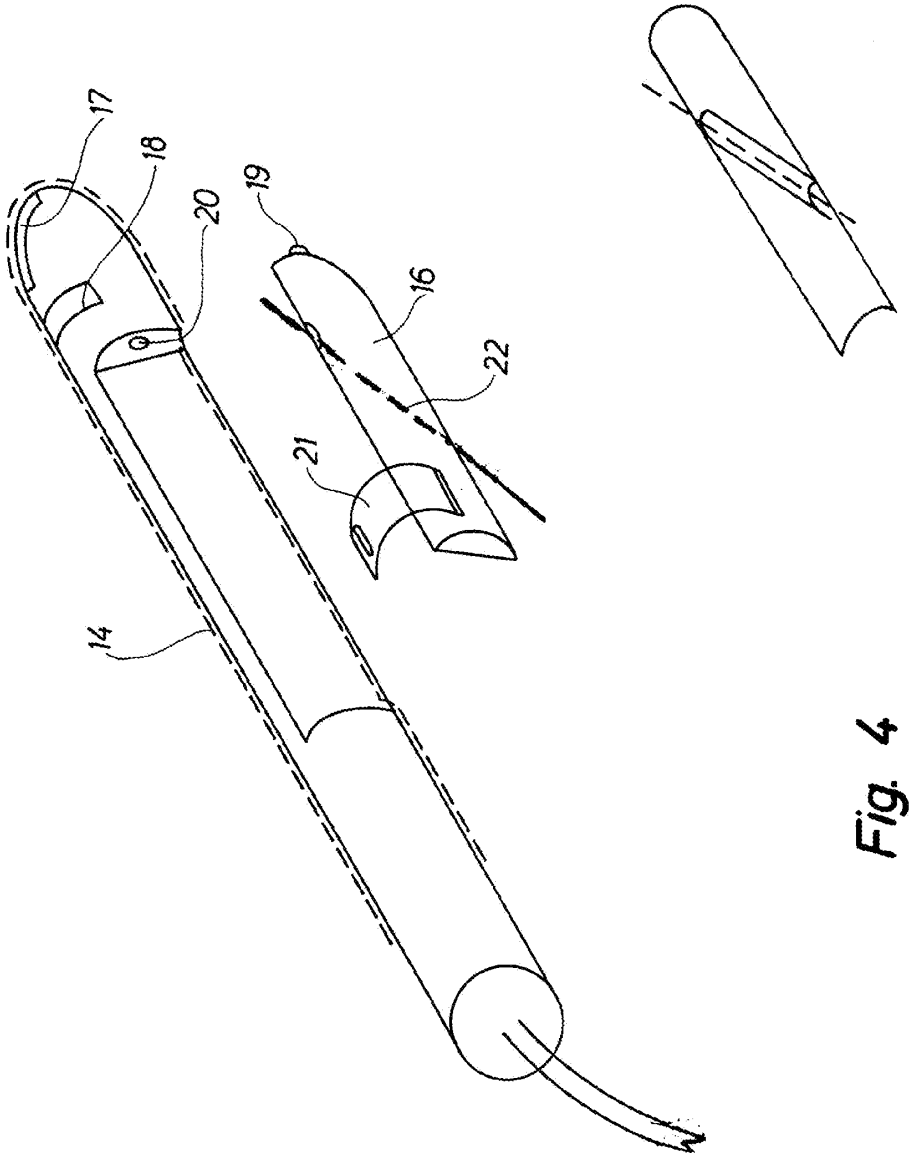


Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00001

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61B 10/00, A61B 8/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPODOC, WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5235987 A (J.K. WOLFE), 17 August 1993 (17.08.93), column 2, line 4 - line 41, figure 1 --	1-5
X	US 4742829 A (W. LAW ET AL.), 10 May 1988 (10.05.88), column 1, line 55 - column 2, line 27, figure 3 --	1-5
A	US 5090414 A (M. TAKANO), 25 February 1992 (25.02.92), figure 8, abstract --	1-5

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 May 1999	15 -05- 1999
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Patrik Blidefalk/AE Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

07/04/99

International application No.
PCT/DK 99/00001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5235987 A	17/08/93	NONE	
US 4742829 A	10/05/88	JP 1870541 C	06/09/94
		JP 4031267 B	26/05/92
		JP 63043648 A	24/02/88
US 5090414 A	25/02/92	JP 1867291 C	26/08/94
		JP 2055050 A	23/02/90

Form PCT/ISA/210 (patent family annex) (July 1992)

Transducer Type 8848

for BK Medical Ultrasound Systems

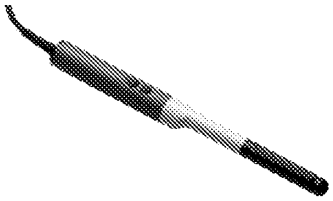
Product Data

USES

- Prostate brachytherapy
- Transrectal imaging
- Transperineal puncture
- Transvaginal imaging
- Prostate cryotherapy
- Spectral and CFM Doppler examinations
- Contrast imaging with Pro Focus 2202*

BENEFITS

- Superior image quality and resolution
- Simultaneous biplane visualization
- Long linear array ideal for dynamic endovaginal imaging of the urethra
- Multifrequency imaging
- Built-in control buttons
- Needle guide for perineal puncture
- Compatible with modern sterilization methods



Transducer 8848

General Description

The 8848 is a simultaneous biplane transducer designed for use with the BK Medical Pro Focus 2202 and Flex Focus 1202 ultrasound systems. It has a convex array for transverse imaging and a linear array for sagittal imaging. These arrays can be used simultaneously for greater orientation and depth information.

The convex array has a sector angle of 140°. With the Expanded Sector feature, the sector angle is widened to approximately 180° providing an even better view.

Applications

The 8848 is designed for transrectal imaging and is particularly useful for prostate brachytherapy and cryotherapy. The 8848 provides a clear picture enabling precise volume studies and assisting in treatment planning.

When using the simultaneous biplane feature, you are able to view two planes at once with a single transducer, and this helps determine the true position of the needle and its tip during puncture and biopsy.

The 8848 is excellent for pelvic floor examinations. Endovaginal imaging, while the patient performs valsalva or squeeze maneuvers, is very useful for a dynamic assessment of the pelvic floor and urethral function.

Interventional Procedures

The UA1232 metal puncture attachment is designed for transperineal puncture of the prostate. It consists of a needle guide and a mounting ring with a lock screw. The needle guide has nine parallel guide channels, spaced 5mm apart, each with an internal diameter of 2.1mm (14gauge). The guide channels are angled at 0° to the transducer's longitudinal axis and 90° to the transverse imaging plane. The needle guide can be adjusted 90mm lengthwise with respect to the mounting ring, using the adjustment screw.

Brachytherapy stepping units are an important accessory to the 8848. The stepping unit allows the transducer to be held stable during perineal puncture, radioactive source implantation and cryotherapy.

The CIVCO AccuCare stepper units (UA2000 and UA2001) are compatible with the 8848.

Multifrequency Imaging

Multifrequency imaging (MFI) is standard on BK Medical systems. The 8848 has a broad bandwidth of 12-4 MHz. It can be used for tissue harmonic imaging and contrast imaging (contrast imaging with the Pro Focus 2202 ultrasound system only).

Cleaning and Disinfection

The 8848 transducer can be disinfected by immersion in the solutions listed under Specifications and can be processed using STERRAD® 50, 100S, 200 systems. The transducer can also be processed using STERIS SYSTEM 1® ** and SYSTEM 1E (when a watertight plug protection device is fitted). UA1232 can be autoclaved.

Sterile transducer covers are available.

Safety

The 8848 is designed and tested in accordance with EN60601-1 (IEC60601-1), "Medical Electrical Equipment, General Requirements for Safety." When used with BK Medical's ultrasound systems, Type BF requirements are met.

* In the USA, contrast-enhanced ultrasound has not been market cleared by the FDA, with the exception of only select cardiac imaging applications.

** STERIS SYSTEM 1 is not market cleared in the USA.

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Specifications 8848

OPERATIONAL FACILITIES
Two built-in control buttons

SAFETY
When used with BK Medical's ultrasound systems, this transducer complies with Safety Standard EN60601-1 (IEC60601-1) Type BF.

FREQUENCY RANGE
12-4MHz (depending on system)

ENVIRONMENTAL
Operating pressure
700-1060 hPa (normal atmospheric pressure)
Operating temperature
+10 to +40 °C (+50to +104 °F)
Storage temperature
-25to+70 °C (-13to+158 °F)
Watertight immersion temperature
Max +40 °C (+104 °F)
Watertight immersion time
Max 15 hours per 24 hours

STERILIZATION AND DISINFECTION
Complete details and procedures can be found in *Care, Cleaning & Safety*.

RESISTANCE TO CHEMICALS AND PROCESSES

Sterilization processing*
8848 can be processed using:
- STERIS SYSTEM 1®** and STERIS SYSTEM 1E
- STERRAD® 50, 100S and 200 Systems

Immersion
For less than 10 minutes in each hour in:
- Chlorhexidine gluconate (5-20%)
- Ethanol (70% in water)
- Isopropanol 70%

For less than 15 hours in each 24 hours in the following solutions:
- Glutaraldehyde (2-3.4% in water)

Wiping
Ethanol (70% in water)

The following disinfectants can also be used (but not exceeding maximum watertight immersion time specified for this transducer):
- Cidex® OPA
- Korsolex® Basic and Extra
- PeraSafe®/ PeraSafe LG
- Tristel®

Follow manufacturer's instructions for use.

POWER SUPPLY
Internally from the system

CABLE LENGTH
2.3 m (7.5 ft)

MANUFACTURER
BK Medical ApS
Mileparken 34
DK-2730 Herlev
Denmark

TRADEMARKS
- STERIS SYSTEM 1 and SYSTEM 1E are registered trademarks of STERIS Corporation.
- STERRAD is a registered trademark of Advanced Sterilization Products (ASP), a Johnson & Johnson Company.
- Cidex OPA is a registered trademark of Advanced Sterilization Products (ASP), a Johnson & Johnson Company.
- Korsolex is a registered trademark of Bode Chemie GmbH.
- PeraSafe is a registered trademark of Antec International.
- Tristel is a registered trademark of Tristel Pharmaceutical.

* Sterilization processes are harsh and can shorten the life of the product.
** STERIS SYSTEM 1 is not market cleared in the USA.

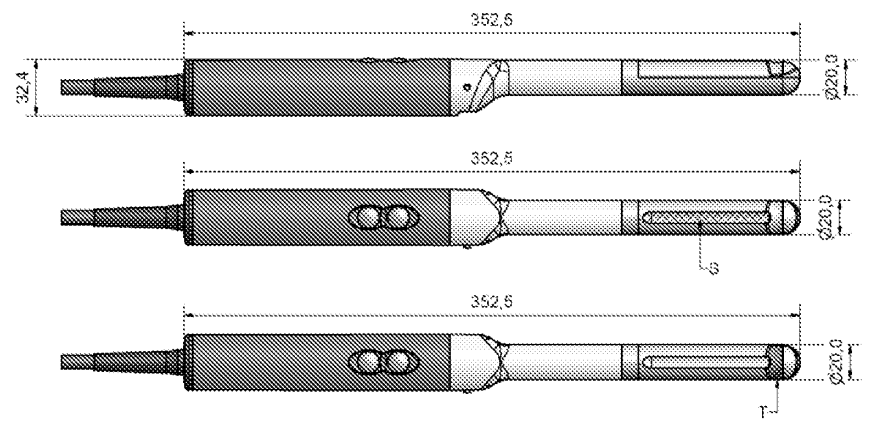
	Units	8848											
		2202						12021					
Imaging Plane		Transverse			Sagittal			Transverse			Sagittal		
B Mode Frequency	MHz	12	9	6	12	9	6	12	9	6	12	9	6
Doppler Frequency	MHz	7.5	6	5	7.5	6	5	7.5	6	5	7.5	6	5
Contrast Frequency	MHz	4.3 4											
Number of Elements		128			192			128			192		
Radius of Curvature	mm	9.3						9.3					
Transverse Plane Aperture	mm	5.5											
Transverse Focal Length	mm	40 (Typical)											
Image Plane Aperture	mm	11.5			21.8			11.5			21.8		
Image Plane Focal Length	mm	Variable											
Axial Resolution*	mm	0.5	0.4	0.5	0.3	0.3	0.4	0.5	0.4	0.5	0.5	0.5	0.5
Lateral Resolution*	mm	1.5	1.5	1.8	0.8	0.9	0.9	1.2	1.3	1.7	1	1	1.1
Image Field		140°			65 mm			140°			65 mm		
B-mode Image Field incl. Expanded Sector		180			65 mm + 15° each side			180			65 mm + 15° each side		
Basic Imaging Modes		B, M, Doppler, CFM, Tissue Harmonic Imaging, Contrast Imaging**											
Penetration Depth*	mm	54	74	83	74	82	103	83	74	80	82	88	100
Focal Range	mm	3-60											
Frame Rate (Max)	Hz	>150											
Contact Surface (Acoustic)	mm	23 x 5.5			65 x 5.5			23 x 5.5			65 x 5.5		
Contact Surface (Overall)	mm	127			357			127			357		
Total Dimensions	mm	352.5 x 32.4											
Size of Handle	mm	150 x 32.4											
Weight (Approximate)	g	250											
Applications (Typical)		Transrectal, Transvaginal											

† Only available on Flex Focus 400 and 700
* Measurements according to IEC/TS 61390 and JIS T 1501. Penetration depth is measured in an ultrasound phantom and recalculated corresponding to a realistic tissue attenuation of 0.5 dB/cm/MHz.
** In the USA, contrast-enhanced ultrasound has not been market cleared by the FDA, with the exception of only select cardiac imaging applications.
For definition of terms, refer to Acoustic Output Measurement for Diagnostic Ultrasound Equipment, AIUM/NEMA 2004.

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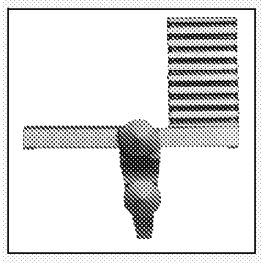
8848 Technical Drawings

All measurements are in mm.



Puncture Attachment UA1232

- Weight: 107 g
- Dimensions: 90 x 90 x 45 mm
- Material: Stainless steel AISI303



Ordering Information 8848

ACCESSORIES AVAILABLE

UA1232:	Puncture Attachment (bore diameter 2.2mm; angle of insertion 0° to the long axis of the transducer)
UA0059:	Endocavity Standoff Kit
UA2000:	CIVCO Classic Stepper and Stand (18G)
UA2001:	CIVCO Classic Stepper and Stand (17G)
UA2010:	EXII Tracked Stepper and Stand (18G)
UA2011:	EXII Tracked Stepper and Stand (17G)
UA0513:	Magnetic Wheel Mover
UA0510	Adapter Ring for use with UA0513
KE4325:	Carrying Case for 8848

TRANSDUCER COVERS

UA0005:	Sterile Latex (pack of 24)
UA0008:	CIV-Flex™ Sterile, latex-free (pack of 24)

TRADEMARKS

CIV-Flex is a trademark of CIVCO Medical Instruments Co., Inc.

- **Headquarters USA** · B-K Medical Systems, Inc. · 8 Centennial Drive, Peabody, MA 01960 · Tel: +1 800 876-7226 / +1 978 326-1300
- **Headquarters Europe and Rest of World** · BK Medical · Mileparken 34, DK-2730 Herlev, Denmark · Tel.: +45 4452 8100

www.bkmed.com *A wholly owned subsidiary of Analogic Corporation*

Endorectal Biplane Transducer Type 8808e

for BK Medical Ultrasound Scanners

Product Data

USES

- Transrectal scanning of the prostate
- Transrectal puncture of the prostate
- Transperineal puncture
- Spectral and CFM Doppler examinations
- Tissue harmonic imaging

BENEFITS

- Superior resolution
- Simultaneous biplane visualization
- Built-in control buttons
- Specially designed built-in transrectal biopsy guide for easier biopsies
- Sterile-packed single-use biopsy guide
- Transperineal puncture guide
- Compatible with modern sterilization methods

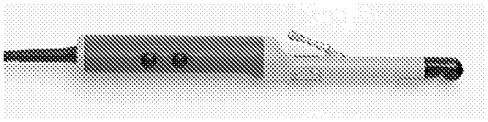


Fig. 1 Biplane transducer 8808e assembled for transrectal puncture

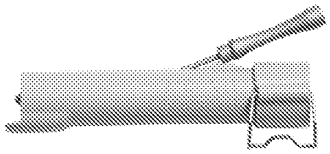


Fig. 2 Simultaneous Biplane Biopsy Guide UA1326

General Description

Type 8808e is a biplane transducer designed for use with BK Medical's Flex Focus 1202 and Pro Focus 2202 UltraView ultrasound scanners. It has two convex arrays, one for transverse scanning and one for sagittal scanning.

Applications

The 8808e is designed for transrectal scanning. It has a dynamic focus extension of 3 to 58 mm in both planes and a sector angle of 126°.

The 8808e is particularly useful for transrectal puncture. The advantage of viewing both the sagittal and transverse planes is that the needle is visible throughout the puncture and biopsy procedures. The transducer includes a simultaneous biplane feature that enables both planes to be visualized live at the same time.

Interventional Procedures

Transrectal Biopsy

Transrectal puncture and biopsy can be performed using simultaneous biplane scanning, where both the sagittal and transverse planes are visualized live at the same time, the advantage is that the needle is visible in both planes throughout the puncture and biopsy procedures. Use reusable biopsy guide UA1326 or sterile-packed single-use UA1322-S.

The biopsy guides have an internal diameter of 1.6mm (17 gauge).

Transperineal Biopsy

The metal puncture attachment UA1324 is designed for transperineal puncture and biopsy. It consists of a needle guide and a mounting ring with a locking clamp.

The needle guide has nine parallel guide channels spaced 5mm apart, each with an internal diameter of 2.1mm (14 gauge). The guide channels are angled at 0° to the transducer's longitudinal axis and 90° to its transverse axis. The needle guide can be adjusted 70mm lengthwise with respect to the mounting ring, using the adjustment screw.

Multifrequency Imaging

The transducer transmits at 5, 6, 8 and 10 MHz. It can be used for tissue harmonic imaging with the Flex Focus and Pro Focus ultrasound scanners.

Cleaning and Disinfection

The 8808e can be disinfected by immersion in the solutions listed under Specifications. The puncture attachments can be disinfected by immersion and can be autoclaved. Single-use biopsy guides are also available.

Sterile transducer covers are available.

Safety

The 8808e is designed and tested in accordance with EN 60601-1 (IEC 60601-1), "Medical Electrical Equipment, General Requirements for Safety." When used with BK Medical's ultrasound scanners, Type BF requirements are met.

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Specifications 8808e

SAFETY:
Complies with Type BF requirements of EN60601-1 (IEC 60601-1)

FREQUENCY RANGE:
5-10 MHz

OPERATIONAL FACILITIES:
Two built-in control buttons

ENVIRONMENTAL:
Operating pressure:
700-1060 hPa (normal atmospheric pressure)
Operating temperature:
+10 to +40°C, (+50 to +104°F)
Storage temperature:
-25 to +70°C, (-13 to +158°F)
Watertight immersion temperatures:
Max. +40°C (+104°F)
Watertight immersion time:
Max. 15 hours per 24 hours

Resistance to chemicals during disinfection:
Immersion for less than 10 minutes in each hour in:
- Chlorhexidine gluconate (5-20%)
- Tristel®
- Korsolex® Basic
- Korsolex® Extra
- PeraSafe®

Immersion in the following solutions, following manufacturer's instructions (but not exceeding maximum watertight immersion time specified for this transducer):
- Glutaraldehyde (2-3.4% in water)
- Cidex OPA™

- Wiping with ethanol or isopropanol (70% in water)

- The 8808e can be processed using STERIS SYSTEM 1® *

POWER SUPPLY:
Internally from scanner

CABLE LENGTH:
2.2m (7.2ft)

TRADEMARKS:
- STERIS and STERIS SYSTEM 1® are registered trademarks of STERIS Corporation.
- Tristel is a registered trademark of Tristel Pharmaceutical.
- Korsolex is a registered trademark of Bode Chemie GmbH.
- PeraSafe is a registered trademark of Antec International.
- Cidex OPA is a registered trademark of Advanced Sterilization Products (ASP), a Johnson & Johnson Company.

* STERIS SYSTEM 1 is not market cleared in the USA

	Units	1202 ††				2202 †			
Scanning planes		Transverse and Sagittal				Transverse and Sagittal			
Center frequency	MHz	5	6	8	10	5	6	8	10
Doppler frequency	MHz	5 - 6 - 7.5				5 - 6 - 7.5			
Tissue Harmonic frequency	MHz	8				8			
Number of elements		2 x 96				2 x 96			
Radius of curvature	mm	9.7				9.7			
Transverse plane aperture	mm	5				5			
Transverse focal length (typical)	mm	25				25			
Image plane aperture	mm	19.6				19.6			
Image plane focal length	mm	variable				variable			
Axial resolution*	mm	0.6(T), 0.3(S)	0.5(T), 0.3(S)	0.5(T), 0.3(S)	0.5(T), 0.3(S)	0.5	0.4	0.4	0.4
Lateral resolution** (measured at 25 mm)	mm	0.3(T), 0.2(S)	0.3(T), 0.2(S)	0.2(T), 0.3(S)	0.2(T), 0.3(S)	1	1	0.6	0.6
Image field		126°				126°			
Basic scanning modes		B, M, Doppler, CFM, Tissue Harmonic Imaging				B, M, Doppler, CFM, Tissue Harmonic Imaging			
Penetration depth**	mm	83(T), 83(S)	72(T), 75(S)	62(T), 65(S)	53(T), 54(S)	105	104	97	83
Focal range	mm	3-58				3-58			
Frame rate (max)	Hz	>200				>200			
Contact surface (acoustic)	mm	5 x 20				5 x 20			
Total dimensions	mm	320 x 32				320 x 32			
Size of handle	mm	135 x 32				135 x 32			
Weight (approximate)	g	250				250			
Applications (typical)		Transrectal				Transrectal			

† Only available on Pro Focus UltraView
†† Not available on Flex Focus 400 Anesthesia
* Transverse axial resolution measured at 27.7 mm and Sagittal axial resolution measured at 25 mm.
** Measurements according to IEC/TS 61390 and JIS T 1501. Penetration depth is measured at 0.7dB/cm/MHz and recalculated corresponding to a realistic tissue attenuation of 0.5 dB/cm/MHz.
For definitions of terms, refer to Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment, AIUM/NEMA, 2004.

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Ordering Information 8808e

ACCESSORIES INCLUDED

UA1325: Dummy channel bracket

ACCESSORIES AVAILABLE

UA1324: Perineal puncture attachment (bore diameter 2.1mm; angle of insertion 0° to the long axis of the transducer)

UA1326 Simultaneous biplane biopsy guide, reusable (bore diameter 1.6 mm; angle of insertion 19° to the long axis of the transducer)

UA1322-S Simultaneous biplane biopsy guide, sterile-packed single-use (pack of 18), (bore diameter 1.6 mm; angle of insertion 19° to the long axis of the transducer

QZ0040: Single-use cleaning brush for needle guide

KE4300: Carrying case

TRANSDUCER COVERS

UA0008: Sterile cable covers (pack of 24) CIV-Flex™

UA0032 Transducer cover (pack of 25) Latex

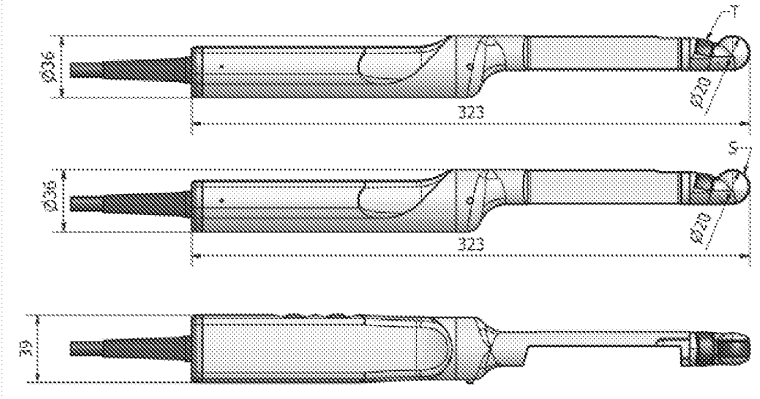
UA0069 Latex covers (pack of 24)

TRADEMARK:

CIV-Flex is a trademark of CIVCO Medical Systems Co., Inc.

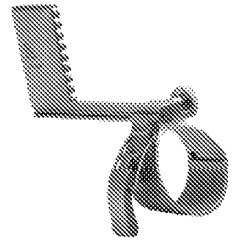
Technical Drawings

All measurements are in mm.



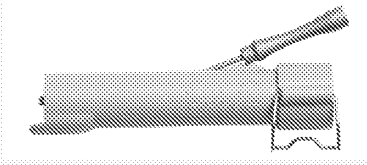
Perineal Puncture guide UA1324

- Weight: 125g
- Dimensions: 101 x 95 x 50mm
- Material: stainless steel AISI303



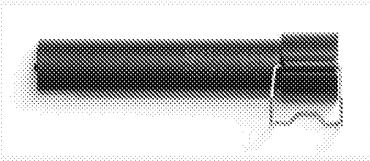
Simultaneous Biplane Biopsy Guide UA1326

- Weight: 21g
- Dimensions: 116 x 42 x 28mm
- Material: PEI (Ultem), stainless steel AISI304 and XCR12Ni17.7



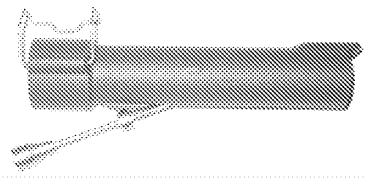
Dummy channel bracket UA1325

- Weight: 11g
- Dimensions: 110 x 24 x 28mm
- Material:PEI (Ultem) and stainless steel XCR12Ni17.7



Simultaneous Biplane Biopsy Guide UA1322-S

- Weight: 14g
- Dimensions: 120 x 45 x 28mm
- Material:ABS (Terlux), Stainless steel AISI304 and XCR12Ni17.7



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Prostate Cancer

Needle Core Length is a Quality Indicator of Systematic Transperineal Prostate Biopsy

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Abstract

Objective: To analyse the length of needle cores sampled as a quality indicator in systematic transperineal prostate biopsy. We assessed the correlation of core length with the other clinical and topographic parameters.

Material and methods: We prospectively evaluated data from 509 consecutive patients who underwent a first set of transrectal ultrasound-guided transperineal prostate biopsy for suspected prostate cancer. Fourteen cores were sampled from each patient. Needle cores were stretched and placed in tissue cassettes between two nylon meshes according to the pre-embedding methods of prostate needle biopsy specimens. For single biopsy core, the measurement of length (in millimetres) and any percentage of cancer in the biopsy specimen were reported.

Results: The mean length of 7,126 analysed cores was 14.14 ± 4.35 mm. All cores were longer than 10 mm. The mean length of needle cores sampled did not correlate with patient age, total prostate-specific antigen value, digital rectal examination, and prostate volume. The whole mean length of the six samples from the peripheral zone of the right lobe was higher than the mean corresponding value of the six samples from the left lobe peripheral zone ($p < 0.001$). The transperineal approach allows a greater sampling of the prostate apex than of the midgland and prostate base ($p < 0.001$).

Conclusions: The length of the needle cores sampled during transperineal prostate biopsy fulfils the parameters of quality required by pathologists for an appropriate evaluation of the biopsy specimen.

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1. Introduction

The length of cores sampled during prostate biopsy is a parameter that can affect prostate cancer detection rate [1,2]. The biopsies provided by the urologists should be of adequate length and quality. A core length >10 mm is usually considered a quality indicator of prostate needle biopsies [2,3]. Shorter than this, the biopsies should be considered inadequate for a correct histological evaluation and not diagnostic [3]. The core length depends on bioptic needle characteristics and may be influenced by the site of specimens sampled and the method of needle core pre-embedding [1,4–6].

Data concerning biopsy core length come from studies that exclusively analyse patients who have undergone transrectal prostate biopsy. Studies that assess the quality of cores sampled during transperineal prostate biopsy are not available in the literature. This lack is understandable considering the limited spread of this latter bioptic technique in the United States and Europe [7].

The transperineal access of the bioptic needle along the prostate longitudinal axis could allow a more effective and selective sampling of the prostate peripheral zone than with the transrectal approach [8,9]. A further advantage of the transperineal approach could be an easier sampling of the anterior zone, which could be particularly useful in the re-biopsy planning [10].

In the present study, we analysed the length of needle cores sampled during transperineal prostate biopsy to verify their responsiveness to quality criteria. We also assessed the correlations between core length and the other clinical and topographic parameters.

2. Materials and methods

From October 2002 to October 2004, we prospectively evaluated data from 509 consecutive patients with suspected prostate cancer who had undergone a first set of transrectal ultrasound (TRUS)-guided transperineal prostate biopsy in our department. All patients provided written consent to perform the procedure and to the use of the clinical and pathological data for clinical field research. International review board approval was not required.

For each patient the following clinical variables were evaluated: age, digital rectal examination, total prostate-specific antigen value, and prostate volumes estimated by TRUS (with the ellipse method: length × depth × width × $\pi/6$). The biopsy was conducted on patients placed in the lithotomy position with a single transperineal access 1.5 cm above the anal sphincter on the median line. In all cases an anaesthetic block of the periprostatic plexus was performed by administering 2 mL of 1% mepivacaine at the prostate apex. A 17-gauge coaxial needle (TruGuide Bard, 13 cm long) was inserted up to the prostate apex through the anesthetised perineal path under TRUS guidance (Siemens Sonoline Omnia Diagnostic Ultrasound System, with a 7.75-MHz linear probe). On the removal of the blunt tip stylet, the guiding cannula of the coaxial needle was used as transperineal metallic path for repeated atraumatic passage of the biopsy needle (Tru-Cut 18 G, cutting length of 23 mm) [11].

Fourteen cores were sampled in every patient: double sextant biopsy from the peripheral zone and two cores from the transitional zone (Fig. 1). Needle cores were stretched and placed in tissue cassettes between two nylon meshes according to the pre-embedding methods of prostate needle biopsy specimens described by Rogatsch et al. [5]. Each sampled core was numbered and identified by site and prostate lobe. The core biopsies were distributed in couples on labelled tissue cassettes. Afterwards the tissue cassettes were submitted in containers filled with 10% buffered formalin. After fixation and dehydration, all tissue cores were embedded in paraffin blocks and then sectioned by histotechnologists. The histologic diagnoses were performed by two expert uropathologists (Guido Martignoni and Maurizio Pea). For a single biopsy core, the length in millimetres and any percentage of cancer in the biopsy specimen were measured. The percentage of cores' fragmentation and the rate of cores without prostatic tissue were reported. The tumour grade differentiation was assigned with the Gleason grading and scoring system.

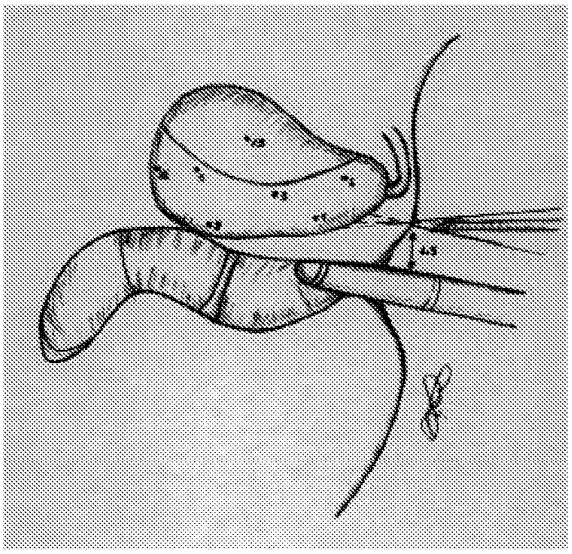


Fig. 1 – site of core sampling at the right prostate's lobe. Cores 1, 3, and 5 correspond to the traditional sextant biopsy protocol. Cores 7, 9, and 11 refer to the additional, peripheral, lateral sextant. Core 13 comes from the transitional zone. The coaxial needle, which allows the atraumatic passage of biopsy needle, is inserted 1.5 cm above the anal sphincter on the median line under local anaesthesia.

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Table 1 – Topographic identification, length, and detection rate of single sampled prostate needle cores

Core number	Lobe	Site	Length (mean ± SD)	Positive diagnosis (%)	% positive core
1	Right	Apex	15 ± 2.3	75 (14.7%)	40 (20–80)
2	Left	Apex	14 ± 2.1	72 (14.1%)	35 (20–80)
3	Right	Mid	15 ± 3.2	103 (20.2%)	40 (15–80)
4	Left	Mid	14 ± 2.8	101 (19.8%)	50 (22–70)
5	Right	Base	14 ± 3.5	85 (16.7%)	40 (10–70)
6	Left	Base	13 ± 2.3	80 (15.7%)	50 (10–80)
7	Right	Apex	15 ± 2.1	87 (17.7%)	55 (20–80)
8	Left	Apex	14 ± 2.0	88 (18.1%)	50 (20–75)
9	Right	Mid	13 ± 3.1	80 (16.8%)	40 (20–70)
10	Left	Mid	12 ± 2.8	87 (18.3%)	40 (20–70)
11	Right	Base	14 ± 3.1	50 (10.3%)	20 (5–50)
12	Left	Base	12 ± 3.3	68 (14.3%)	20 (10–50)
13	Right	Transition zone	15 ± 2.8	35 (7.3%)	30 (10–50)
14	Left	Transition zone	15 ± 2.7	46 (9.7%)	40 (20–70)

2.1. *Statistical analysis*

All data were collected in a database and analysed with Statistical Package for Social Sciences, version 10.1, software by Vincenzo Ficarra. The Pearson chi-square test was used to compare categorical variables. The Mann–Whitney test or the Kruskall–Wallis H test was used to compare two or more continuous nonparametric variables, respectively. All p values were two sided and a $p < 0.05$ was considered significant.

3. Results

Patients were of a mean age of 66 ± 7.5. PSA median value was 7.1 ng/mL (interquartile range 5.2–9.7 ng/mL). The prostate median volume was 37 cc (interquartile range 26.9–50.9 cc). Digital rectal examination findings were positive in 177 cases (34.8%). The mean length of 7,126 analysed cores was 14.14 ± 4.35 mm. All cores were longer than 10 mm. Only 216 cores (3%) were fragmented. The absence of prostatic tissue was reported in only 28 cores (0.4%).

Table 1 reports the mean values ± standard deviation (SD) of the length of single cores sampled. The mean length of needle cores sampled did not correlate with patient age, total PSA value, digital rectal examination, and prostate volume (Table 2).

Regarding the prostate topography, the whole mean length of the six samples from the peripheral zone of the right lobe was 86.59 ± 21.4 mm. The mean corresponding value of the six samples from the left lobe peripheral zone was 79.98 ± 18.59 mm ($p < 0.001$). Concerning the site, the total mean length of the cores sampled was 64.64 ± 11.14 mm at the apex, 55.26 ± 14.53 at the midgland, and 54.94 ± 14.22 mm at the base ($p < 0.001$). Moreover, the mean value of the sum of samples corresponding to traditional sextant was 84.92 ± 19.89 mm. This value was significantly higher than that calculated at the more lateral sextant level ($p = 0.005$) (Table 2).

Altogether, the 14-core scheme allowed the diagnosis of 232 (45.6%) prostate cancers. The Gleason score did not apply to 32 cases (13.8%) (<5% of positive single core). In the remaining 200 patients the Gleason score was 5 in one case (0.5%); 6 in 115 cases (57.5%); 7 in 41 (20.5%); 8 in 24 (12%); 9 in 13 (6.5%), and 10 in six (3%) (Fig. 2). In every

Table 2 – Correlation between mean length of sampled cores and clinical and topographic variables

Variable	Total core length (mean value ± standard deviation)	P value
Age (years)		0.27
- ≤50 ($n = 10$)	169.40 ± 33.44	
- 50.1–60 ($n = 113$)	162.12 ± 38.50	
- 60.1–70 ($n = 247$)	169.18 ± 36.57	
- >70 ($n = 139$)	165.36 ± 35.56	
Digital Rectal Examination		0.73
- negative ($n = 332$)	165.95 ± 37.02	
- positive ($n = 111$)	167.74 ± 35.76	
Total PSA (ng/mL)		0.32
- ≤10	167.01 ± 35.95	
- 10.1–20	162.33 ± 41.49	
- >20	174.10 ± 26.22	
Prostate volume (mL)		0.32
- ≤30	170.05 ± 36.75	
- 30.1–40	166.48 ± 37.85	
- 40.1–50	163.91 ± 35.31	
- >50	163.92 ± 35.82	
Lobe		0.001
- right	86.59 ± 21.4	
- left	79.98 ± 18.5	
Site		0.001
- apex	64.64 ± 11.14	
- midgland	55.26 ± 14.53	
- base	54.94 ± 14.22	
Peripheral zone		0.005
- traditional sextant	84.92 ± 19.89	
- lateral sextant	81.65 ± 19.64	

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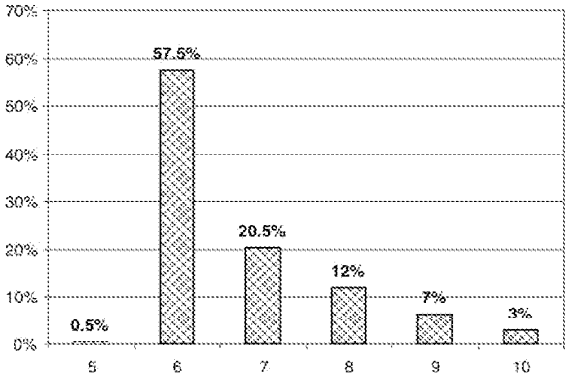


Fig. 2 – Distribution of the Gleason score in the 200 patients with diagnosis of prostate cancer. The Gleason score was not assigned in 32 patients with a single microscopic focus of prostate cancer (<5% within a single core).

sampling site, the mean length of needle cores positive and negative for adenocarcinoma statistically overlapped (Table 3). Similar results were observed when we considered the whole length of cores sampled from the right lobe ($p = 0.59$), the left lobe ($p = 0.11$), the prostate apex ($p = 0.22$), the midgland ($p = 0.06$) and the base ($p = 0.12$) (Table 4).

4. Discussion

The mean length of needle cores sampled during transperineal systematic prostate biopsy proved to be up to the best qualitative standards reported in the literature. This morphometric parameter was not influenced by patients' clinical characteristics. On the contrary, statistically significant differences emerged in relation to sampling site and side. In particular, the mean lengths of the cores sampled from the left lobe was lower than those sampled from the right. Also, the whole length of the cores sampled from the midgland or base was lower than those sampled at the prostate apex. Moreover, the length of biopsy cores, negative and positive at histology overlapped for each single sample site and for both site and lobe, after core clustering.

The length of the cores might be influenced by the methodology used to collect them. The pre-embedding technique was considered the best strategy to yield a good standard of quality [5]. We elected to use this method as our current clinical practice from the beginning of this study. The length of prostate cores is considered a quality indicator of prostate needle biopsy [2,3]. However, according to a recent survey performed among 110 urologists from France and Belgium, the length of the cores was not considered among the most relevant data in the clinical practice [12].

The quality of needle cores obtained by transperineal approach may be considered along with that observed after transrectal prostate biopsy. Data from transrectal prostate biopsies performed within the Tyrol screening project showed that after the pre-embedded method the mean length of positive cores was 13.17 mm [5]. Similarly, in a multicentre American series, the mean length of cores sampled from 1,847 patients who underwent transrectal prostate biopsy was 12.8 ± 3.5 mm [1]. In the comparative study by Emiliozzi et al., the length of cores obtained by transperineal and transrectal

Table 3 – Comparison of positive and negative biopsy core mean lengths. Analysis made per single point of biopsy sampling

Core Number	Positive core length (mm)	Negative core length (mm)	P value
1	15.73 ± 6.40	14.43 ± 5.14	0.23
2	14.47 ± 3.73	13.61 ± 4.85	0.07
3	16.15 ± 6.10	14.64 ± 5.17	0.06
4	14.76 ± 4.28	13.92 ± 4.46	0.16
5	15.05 ± 5.70	14.54 ± 5.39	0.52
6	13.70 ± 4.00	12.77 ± 4.35	0.12
7	14.98 ± 4.34	14.35 ± 5.15	0.27
8	13.53 ± 4.00	13.56 ± 4.38	0.86
9	14.51 ± 5.31	14.10 ± 4.97	0.76
10	13.43 ± 4.78	12.73 ± 6.70	0.14
11	14.94 ± 6.33	14.53 ± 5.42	0.60
12	13.93 ± 5.25	12.67 ± 4.55	0.72
13	15.40 ± 5.84	15.21 ± 5.00	0.97
14	14.41 ± 5.15	14.84 ± 4.66	0.27

Table 4 – Mean values of total length of cores sampled from each prostate lobe (right and left) and each prostate site (apex, midgland, base) stratified by histology

Parameter	Cases (%)	Total core length (mean ± SD)	P value
Right lobe			0.59
- positive biopsies	177 (34.7%)	88.8 ± 20.32	
- negative biopsies	332 (65.3%)	88.4 ± 21.92	
Left lobe			0.11
- positive biopsies	170 (33.4%)	81.71 ± 17.02	
- negative biopsies	339 (66.6%)	79.12 ± 19.29	
Apex			0.22
- positive biopsies	165 (32.4%)	65.53 ± 10.1	
- negative biopsies	344 (67.6%)	64.21 ± 11.5	
Midgland			0.06
- positive biopsies	185 (36.3%)	56.71 ± 13.17	
- negative biopsies	324 (63.7%)	54.43 ± 15.21	
Base			0.12
- positive biopsies	156 (30.6%)	56.46 ± 13.96	
- negative biopsies	353 (69.4%)	54.28 ± 14.30	

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biopsy sextant overlapped [9]. The inferior length of cores sampled from the left of the median line might be explained by the fact that the operators who extract the sample were all right-handed, and so had to execute the manoeuvre in the direction opposite to the natural one. These morphometric data did not affect the detection rate, which overlapped in each prostate lobe.

Iczkowski et al. observed that the length of cores sampled during transrectal prostate biopsy was longer at the midgland and base than at the prostate apex [1]. Currently, similar evaluations in transperineal prostate biopsy series are not available. On the contrary, the data from our study underline that the transperineal approach allows a better sampling at the prostate apex than at the midgland and prostate base. Moreover, the mean length of each core sampled at the level of these two prostate portions is substantially similar to that reported in the study carried out in Pennsylvania and Virginia after transrectal biopsy [1].

In an experimental study conducted on radical prostatectomy specimens, Vis et al. showed how the needle access at the prostate apex level and its longitudinal path could allow a more effective and selective sampling of prostate peripheral zone than that of the transrectal approach [8]. The execution of the far lateral samples at the peripheral zone of the prostate needs a greater inclination of the needle towards prostate longitudinal axis. This issue explains the significant difference in core length identified between the cores sampled from traditional sextant and those from the lateral sextant. Moreover, a similar result was reported by Terris et al. in 1997 with a transrectal approach [4].

Some authors proved a direct correlation between needle core length and prostate cancer detection rate [1,2]. A possible explanation may be linked to the adequacy of histologically negative specimens [3]. In our study the mean length of negative cores was always longer than quality standards and similar to that of cores with a diagnosis of cancer. The percentage of fragmented cores and the rate of cores without prostatic tissue can be considered as further quality indicators. In our study, those figures were 3% and 0.4%, respectively, significantly lower than previously reported in series of transrectal biopsies [6,13].

A previous paper of ours showed that transperineal prostate biopsy guaranteed low rate of severe complications, such as fever (0.6%), acute urinary retention (0.6%), and perineal haematoma (0.3%) [14]. In fact, haemospermia occurred in 53% of patients and haematuria in 59% of patients [11].

5. Conclusions

The length of the needle cores sampled during transperineal prostate biopsy fulfils the parameters of quality required by pathologists for an appropriate evaluation of the biopsy specimen. The transperineal approach allows a greater sampling of the prostate apex than of the midgland and prostate base. Nevertheless, these portions are adequately sampled. The mean lengths of needle cores sampled transperineally and those reported by the major literature series that used the transrectal approach substantially overlap.

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ELSEVIER

PAIN ASSESSMENT AFTER ORIGINAL TRANSPERINEAL PROSTATE BIOPSY USING A COAXIAL NEEDLE

GIOVANNI NOVELLA, VINCENZO FICARRA, ANTONIO GALFANO, RICCARDO BALLARIO, GIACOMO NOVARA, STEFANO CAVALLERI, AND WALTER ARTIBANI

ABSTRACT

Objectives. To assess whether the use of a coaxial needle reduces discomfort in patients undergoing multiple-core transperineal prostate biopsy to detect prostate cancer.

Methods. From October 2002 to January 2003, we enrolled 102 consecutive patients with a suspicion of prostate cancer. In every case, we performed a 14-core transperineal prostate biopsy under transrectal ultrasound guidance. The patients were randomized into two groups: group 1 (n = 51) in which we used the 17-gauge coaxial TruGuide needle, and group 2 (n = 51) in which the conventional transperineal technique was used. At the end of the procedure, patients were asked to complete a questionnaire regarding the level of pain experienced.

Results. The studied groups were comparable in age, total prostate-specific antigen value, and prostate volume. The whole procedure was significantly less painful in group 1 (2.20 ± 1.20 versus 2.90 ± 1.73, $P = 0.01$). We failed to show any significant pain score differences during rectal probe insertion ($P = 0.10$), transrectal ultrasonography ($P = 0.16$), and execution of local anesthesia ($P = 0.11$). The pain score recorded during the multiple-core prostate sampling was significantly lower in group 1 (1.53 ± 1.5 versus 2.43 ± 1.86, $P = 0.009$). No statistically significant differences were found in the complication rates between the two groups.

Conclusions. The use of a coaxial needle reduces the procedure's invasiveness and patient's pain compared with the conventional transperineal prostate biopsy. UROLOGY **62:** 689–692, 2003. © 2003 Elsevier Inc.

The transrectal ultrasound (TRUS)-guided transperineal prostate biopsy is a simple and well-tolerated procedure with a low complication rate. This technique allows optimal sampling of the peripheral and transition zones of the prostate with a greater detection rate.[1] In recent years, the transperineal approach for prostate biopsy has had more limited diffusion than transrectal biopsy, probably because of the supposed greater invasiveness and execution complexity.

In the conventional transperineal technique, the needle is repeatedly inserted through the perineal plane under local anesthesia. To minimize the invasiveness, we recently introduced the use of a 17-gauge coaxial needle (TruGuide Bard) in our clinical practice. The use of coaxial needles has been described for liver, kidney, pancreas, and breast biopsies.[2–4] However, to the best of our knowledge, this is the first experience concerning the utility of this device for prostate biopsy.

The insertion of the coaxial needle up to the prostate apex and the successive blunt tip stylet removal allow the creation of an optimal transperineal path for repeated atraumatic passage of the biopsy needle.

The purpose of the present study was to evaluate whether the use of this new device results in a reduction in the pain patients experience during multiple-core prostate biopsy compared with during the traditional transperineal approach.

MATERIAL AND METHODS

From October 2002 to January 2003, we enrolled 102 consecutive patients with a suspicion of prostate cancer (prostate-specific antigen greater than 4 ng/mL and/or positive digital rectal examination findings). All patients underwent TRUS-guided transperineal prostate biopsy. The patients were adequately informed of mode of execution of the procedure and

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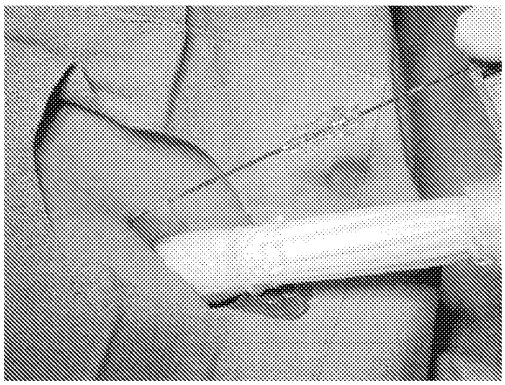


FIGURE 1. *An 18-gauge Tru-Cut biopsy needle on a spring-loaded biopsy gun is inserted into the guiding cannula of the coaxial needle.*

its potential complications and were asked to provide written consent. Internal review board approval was not required at our institution to perform this type of study.

The patients were randomized into two groups in relation to the use of the coaxial 17-gauge TruGuide needle during prostate biopsy. We used the coaxial needle in 51 patients (group 1) and carried out the conventional transperineal technique in the other 51 patients (group 2). In both groups, we evaluated age, digital rectal examination findings, total prostate-specific antigen value, and prostate volumes as estimated by TRUS (with the ellipse method: length $\times$ depth $\times$ width $\times$ $\pi/6$).

Bioptical Technique

All patients stopped anticoagulant therapy 7 days before the procedure and took a prophylactic antibiotic (fluoroquinolone or co-trimoxazole) 12 hours before. An enema was given the same morning of the procedure.

All biopsies were performed by a single urologist (G.N.). TRUS was carried out using the Siemens Sonoline Omnia Diagnostic Ultrasound System, with a 7.75-MHz linear probe. The patient was placed in the lithotomy position, and the perineal area was disinfected. A single, 22-gauge spinal needle was inserted transperineally 1.5 cm above the rectum on the median line. The needle passage through perineal planes was guided by TRUS.

The needle was introduced posteriorly to the bulbar urethra up to the prostate apex and laterally to the membranous urethra. In this area, 2 mL of 1% mepivacaine was released. The needle was progressively retracted and 2 mL of anesthetic was administered along the needle path. An identical procedure was done contralaterally through the same median hole. In group 1, a 17-gauge coaxial needle (TruGuide Bard, 13 cm long) was inserted up to the prostate apex through the anesthetized perineal path under TRUS guidance. On the removal of the blunt tip stylet, the guiding cannula of the coaxial needle was an optimal transperineal path for repeated atraumatic passage of the biopsy needle (18-gauge Tru-Cut, 20 cm long), loaded on a spring-driven biopsy gun (Magnum Bard Biopsy Instruments) with a cutting length of 22 mm (Fig. 1).

In group 2, the same biopsy needle was repeatedly inserted through the anesthetized perineal plane, according to the conventional transperineal technique.

Fourteen cores were sampled in every patient (double sextant biopsy from the peripheral and two cores from the transition zone). The progression and inclination of the needle was controlled by transverse and longitudinal TRUS, respectively. In both groups, at the end of the sampling, an ice bag was placed on the perineal area for about 15 minutes. All the procedures were performed on an outpatient basis.

At the end of the biopsy, every patient received an institutional questionnaire to assess the level of pain during the different steps of the procedure. Thorough instructions for form compilation were provided. The form consisted of six questions:

1. How painful was the whole procedure?
2. How painful was the probe insertion?
3. How painful was the presence of the probe during the procedure?
4. How painful was local anesthetic administration?
5. How painful was the prostate sampling?
6. If medically necessary, how willing would you be to repeat the procedure?

The pain level was evaluated by a visual analog scale/numeric analog scale), in which 0 corresponds to "no pain" and 10 to "the worst pain imaginable."[5] A total pain score of 0 was evaluated as "no pain," a score from 1 to 4 as "mild pain," a score from 5 to 7 as "moderate pain," and any score greater than 7 as "severe pain."[6] For question 6, 0 corresponded to "very willing" and 10 to "never, for no reason."

All patients were clinically evaluated 30 days after biopsy to record the complications related to the procedure.

The Pearson chi-square test and the Student *t* test was used to compare categorical and continuous variables, respectively. In statistical analysis, a $P < 0.05$ was considered significant. The data were collected in a database and analyzed using Statistical Package for Social Sciences, version 10.1, software by one of us (V.F.).

RESULTS

The analyzed groups were comparable in age, digital rectal examination findings, prostate volume, and total prostate-specific antigen value (Table I). The whole procedure (question 1) was significantly less painful in group 1 (2.2 ± 1.20 versus 2.90 ± 1.73, $P = 0.01$). In group 1, 49 (96.1%) had mild pain and 2 (3.9%) had moderate pain. No group 1 patients reported a score greater than 6. In group 2, 42 patients (82.4%) recorded mild pain, 8 (15.6%) moderate pain, and 1 (2%) severe pain (Table II).

For the different procedure steps, we failed to show any statistically significant pain score differences during rectal probe insertion (question 2; $P = 0.10$), TRUS (question 3; $P = 0.16$), or local anesthesia execution (question 4; $P = 0.11$). The pain scores concerning the multiple-core prostate sampling were significantly different. The mean score (question 5) was 1.53 ± 1.51 in group 1 and 2.43 ± 1.86 in group 2 ($P = 0.009$). During this step, 14 patients (27.5%) in group 1 (coaxial needle technique) had no pain, 35 (68.5%) had mild pain, and 2 (4%) had moderate pain. In group 2 (conventional transperineal technique), only 6 patients (11.8%) recorded no pain during the prostate sampling step; 37 (72.5%) reported mild pain, 7 (13.7%) moderate pain, and 1 (2%) severe pain (Table II).

The mean score for question 6 was 2.16 ± 1.60 in group 1 and 3.06 ± 2.14 in group 2 ($P = 0.01$).

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TABLE I. *Clinical characteristics*

Variable	Group 1 (n = 51)	Group 2 (n = 51)	*P* Value
Mean age (yr)	63.76 ± 7.14	65.90 ± 7.54	0.14
Positive DRE (%)	27.5	39.2	0.20
Total PSA (ng/mL)	7.88 ± 3.37	9.26 ± 8.42	0.28
Prostate volume (cm^3)	46.74 ± 27.68	41.81 ± 21.35	0.31

KEY: DRE = digital rectal examination; PSA = prostate-specific antigen.

TABLE II. *Difference in subjective measures between studied groups*

	Group 1 (%)	Group 2 (%)
Whole procedure		
No pain (0)	0	0
Mild pain (1–4)	49 (96.1)	42 (82.4)
Moderate pain (5–7)	2 (3.9)	8 (15.6)
Severe pain (>7)	0	1 (2)
Multiple-core sampling		
No pain (0)	14 (27.5)	6 (11.8)
Mild pain (1–4)	35 (68.5)	37 (72.5)
Moderate pain (5–7)	2 (4)	7 (13.7)
Severe pain (>7)	0	1 (2)

TABLE III. *Mean score (± standard deviation) recorded for each question*

Question	Group 1 (n = 51)	Group 2 (n = 51)	*P* Value
(1) Whole procedure	2.20 ± 1.20	2.90 ± 1.73	0.01
(2) Probe insertion	1.02 ± 1.27	1.43 ± 1.30	0.10
(3) TRUS	1.02 ± 1.34	1.41 ± 1.45	0.16
(4) Local anesthesia	2.29 ± 1.31	2.80 ± 1.87	0.11
(5) Multiple-core sampling	1.53 ± 1.51	2.43 ± 1.86	0.009
(6) Procedure repetition	2.16 ± 1.60	3.06 ± 2.14	0.01

KEY: TRUS = transrectal ultrasonography.

Table III summarizes the reported scores for each question.

The complication rates overlapped in both groups (Table IV).

TABLE IV. *Reported complications (30 days after prostate biopsy; chi-square = not statistically significant in any case)*

Complication	Group 1 (n = 51)	Group 2 (n = 51)
Perineal hematoma	0	1 (2)
Hematuria (lasting >3 days)	30 (59)	23 (45)
Hemospermia	27 (53)	24 (47)
Acute urinary retention	0	3 (6)
Urinary tract infection	0	3 (6)
Fever (>38°C)	0	1 (2)

Numbers in parentheses are percentages.

COMMENT

The TRUS-guided transperineal prostate biopsy is a suitable alternative to the more widespread transrectal approach. The transperineal approach with external ultrasound guidance has been proposed as the optimal way to perform prostate biopsy, mainly in patients who have undergone abdominoperineal resection.[7] Recently, Emiliozzi *et al.*[1] showed that the transperineal technique allowed optimal prostate sampling and had relevant cancer detection rates with acceptable morbidity also in patients who had not undergone any previous abdominoperineal resection. In the transperineal approach, the needle is inserted through the prostate apex along a longitudinal plane parallel to the prostate axis. This eases the needle orientation and provides optimal sampling of the peripheral and transition zones.

Systematic transperineal prostate biopsies need local anesthesia. Although the use of local anesthesia has not been considered mandatory in transrectal prostate biopsy, an increasing number of reports have been showing a relevant reduction of discomfort in patients undergoing transrectal prostate biopsy with local anesthesia.[6,8–10] The prostatic plexus block is the most commonly used technique of local anesthesia during transrectal prostate biopsy. Since the first report of Costello and Costello,[11] several technical modifications have been proposed, mainly involving the dosage and sites of anesthetic injection.[10–13] A recent prospective, randomized study showed that an anesthetic injection at the level of the prostate apex was easier, less painful, and more effective than prostatic plexus block during transrectal prostate biopsy.[6] To administer local anesthesia and to perform transperineal biopsies, double-sided access is often used, on both the left and the right of the median line, 1.5 cm above the rectum, on a line at a 45° angle with the median line.[1] The transperineal access further simplifies anesthetic injection at the prostate apex.

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The use of a single median transperineal access was described by Milani *et al.*[14] Although it involves a greater risk of bulbar urethra injury, this approach allows the reduction of bulbourethral artery injuries and perineal hematoma development and increases procedure tolerability.[14]

To the best of our knowledge, the use of a coaxial needle has not been reported during prostate biopsy. This device makes the procedure easier and quicker. The guiding cannula forms an optimal transperineal path, allowing the repeated insertion of the needle with lower perineal invasiveness and avoiding continual ultrasound control of the needle.

Our data showed that the use of a coaxial needle significantly reduced the experienced pain during prostate sampling and improved patient compliance compared with the conventional transperineal biopsy technique. Our results support the widespread use of a coaxial needle during transperineal prostate biopsy.

An additional possible issue could be the comparison between the use of the perineal coaxial needle and the standard TRUS-guided biopsy. No data are currently available about this topic. Indirect evidence could be gained by comparing our data with those recently published by Stirling *et al.*[15] in a group of 50 patients undergoing TRUS-guided biopsy with periprostatic nerve blockade. Using a similar question about discomfort during prostate sampling and the same visual analog pain scale, the investigators reported a mean score of 2.8 $\pm$ 1.9, significantly greater than our score ($P < 0.001$). Moreover, although in the patients in the study by Stirling *et al.,* a mean number of nine cores was sampled, we performed 14 biopsies in every patient. However, this issue could be better assessed by a randomized prospective trial.

The role of transperineal approach might become more relevant as acceptance of an increase in the number of cores needed to maximize prostate cancer detection rates grows.

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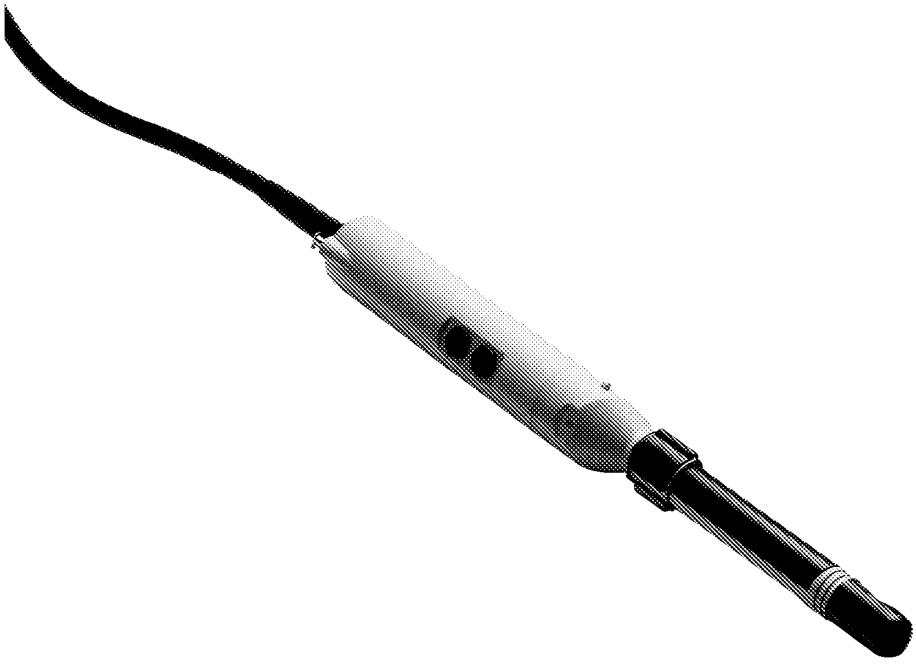
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User Guide

Type 8808

Biplane Transducer



English
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Introduction

This is the user guide for Biplane Transducer Type 8808 and must be used together with *Care, Cleaning & Safety* which contains important safety information.

Indications for Use

Biplane Transducer Type 8808 is designed for transrectal prostate imaging.

Puncture attachment UA1232 and biopsy guide UA1257 provide guidance for needles or other interventional devices during an ultrasound-guided procedure. UA1232 and UA1257 position the needle relative to the transducer, so that the needle image is in a specified position in the ultrasound image during procedures that require precise needle placement or biopsy.

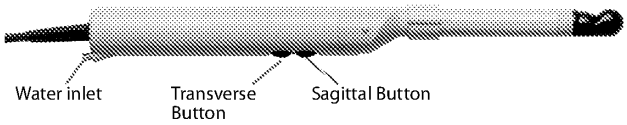


Figure 1. Biplane Transducer Type 8808.

Imaging Plane

The transducer contains two convex arrays — one for transverse (T) imaging, and one for sagittal (S) imaging (see Figure 2). The advantage of being able to view two planes simultaneously with one transducer is that the true position of the needle can be seen during puncture and biopsy and a suspicious lesion can be viewed in both planes.

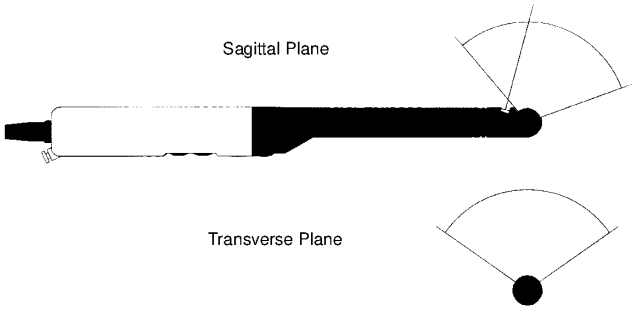


Figure 2. Imaging plane for Biplane Transducer Type 8808.

To image in one plane or the other, press the built-in transducer control button corresponding to that plane (see Figure 1). Pressing the button activates or freezes imaging in the plane.

NOTE: *Some instructions in the "Starting Imaging" chapter refer to a single transducer control button. For the 8808, these instructions refer to each of the control buttons. Which button to use depends on the imaging plane you want to use.*

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Simultaneous Biplane Imaging with 2202 system

1. The transducer can transmit transverse (T) and sagittal (S) images simultaneously. When you press the systems's **Split** button, simultaneous live transmission is automatically activated. On the screen, this is indicated by a green dot in front of the **Simultan** button.
2. Click on **Simultan** to toggle simultaneous live transmission on or off. When simultaneous transmission is *off*, you can change which plane is active and which is frozen by pressing the **Split** button or by placing the cursor on the image you want to be active and pressing the **Select** button.

Imaging Without Puncture or Biopsy

When the 8808 is used for imaging without the puncture facilities, the dummy channel bracket UA1272 must be in place. This clicks into position on the transducer to cover the open channel (see Figure 3).



Figure 3. The 8808 and the dummy channel bracket.

NOTE: *The dummy channel bracket must be removed before the transducer is prepared for disinfection. The bracket can be disinfected using the same methods as explained later under "Puncture and Biopsy Facilities".*

General Information

Product specifications for this transducer can be found in the Product Data sheet that accompanies this user guide.

Acoustic output data and data about EMC (electromagnetic compatibility) for this transducer are in Technical Data (BZ2100) that accompanies this user guide. A full explanation of acoustic output data is given in your system user guide.

WARNING

If at any time the system malfunctions, or the image is severely distorted or degraded, or you suspect in any way that the system is not functioning correctly:

- Remove all transducers from contact with the patient.
- Turn off the system. Unplug the system from the wall and make sure it cannot be used until it has been checked.
- Do not try to repair the system yourself.
- Contact your BK Medical representative or hospital technician.

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WARNING

Always keep the exposure level (the acoustic output level and the exposure time) as low as possible.

Service and Repair

WARNING

Service and repair of BK Medical electromedical equipment must be carried out only by the manufacturer or its authorized representatives. BK Medical reserves the right to disclaim all responsibility, including but not limited to responsibility for the operating safety, reliability and performance of equipment serviced or repaired by other parties. After service or repairs have been carried out, a qualified electrical engineer or hospital technician should verify the safety of all equipment.

Caring for the Transducer

The transducer may be damaged during use or processing, so it must be checked before use for cracks or irregularities in the surface. It should also be checked thoroughly once a month following the procedure in *Care, Cleaning & Safety*.

Cleaning and Disinfection

To ensure the best results when using BK Medical equipment, it is important to maintain a strict cleaning routine.

Full details of cleaning and disinfection procedures can be found in *Care, Cleaning & Safety* that accompanies this user guide. A list of disinfectants and disinfection methods that the transducer can withstand are listed in the Product Data sheet.

Sterile covers are available. See the Product Data sheet for more information.

WARNING

Users of this equipment have an obligation and responsibility to provide the highest degree of infection control possible to patients, co-workers and themselves. To avoid cross contamination, follow all infection control policies for personnel and equipment established for your office, department, or hospital.

Caution: Do not stick anything into the water inlet to clean it. Poking something into this hole can damage the water channel inside the transducer. You can clean the water channel by flushing it with water soon after use, before any foreign matter such as imaging gel has a chance to harden.

Starting Imaging

All equipment must be cleaned and disinfected before use.

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Connecting the Transducer

WARNING

Keep all plugs and sockets absolutely dry at all times.

The transducer is connected to the system using the array Transducer Socket on the system. To connect, the transducer plug's locking lever should first be in a horizontal position. Align the plug to the system socket and insert securely. Turn the locking lever clockwise to lock in place.

When connected, the transducer complies with Type B requirements of EN60601-1 (IEC 60601-1).

Changing Frequency

The Multi-Frequency Imaging (MFI) facility enables you to select the imaging frequency. See the applicable system user guide for instructions. The selected frequency is displayed at the top of the screen.

Using a Transducer Cover

The transducer should be enclosed in a transducer cover or a standard condom. See the Product Data sheet for a list of available transducer covers.

WARNING

Because of reports of severe allergic reactions to medical devices containing latex (natural rubber), FDA is advising health-care professionals to identify their latex-sensitive patients and be prepared to treat allergic reactions promptly.

Apply sterile gel to the tip of the transducer or fill the cover with 1 to 2 ml of sterile water. This improves the screen images by preventing image artifacts caused by air bubbles.

Pull the transducer cover over the transducer.

Gel also creates a good acoustic contact between the skin and the transducer; therefore, apply a small amount to the outside of the cover prior to imaging. Re-apply the gel frequently to ensure good screen images.

WARNING

Use only water-soluble agents or gels. Petroleum or mineral oil-based materials may harm the cover material.

Using the Transducer Control Button

The control button on the transducer controls the imaging.

Press the button to **Start** or **Stop** imaging (freeze frame). Press the button for more than one second to make a copy of the image.

The transducer makes a "beep" sound each time you press the button.

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Changing Orientation

To change the orientation of the image on the monitor, refer to the applicable system user guide for instructions.

Imaging with Type 8808

The 8808 is designed for simultaneous biplane imaging of the prostate.

Assembling the Transducer for Transrectal Use

The 8808 can be equipped with a water standoff facility to improve contact and field of view during transrectal imaging of the prostate. A rubber sheath is mounted on the end of the transducer and filled with water to ensure good acoustic contact with the rectal wall. By varying the amount of water in the sheath, it is possible to alter the position of the transducer's focal zone in the tissue.

If the water standoff facility is required, it is assembled as illustrated in Figure 4 and described as follows:

1. Mount the rubber sheath UA0799 on the transducer and roll it down until it covers the groove *farthest* away from the tip of the transducer.
2. Pull O-ring UA0210 over the rubber sheath and position in the groove *nearest* the tip of the transducer (Picture 2). The O-ring holds the rubber sheath securely in place.
3. Attach a connecting tube with a Luer Lock™ and a 3-way tap to the water standoff inlet (Picture 3) and fill the rubber sheath with water using a standard disposable syringe (Picture 4).

Air bubbles may appear in the rubber sheath. As air bubbles will disrupt the path of the ultrasound beam and cause image artifacts, they must be removed.

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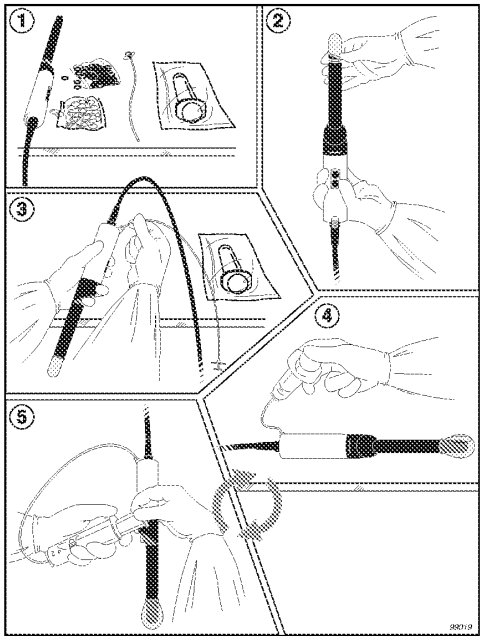


Figure 4. Assembly of the water standoff facility.

4 To remove all air from the rubber sheath, hold the transducer horizontally with the control buttons facing left (water inlet upwards). Then, using the syringe, draw off as much air as possible. You may have to tilt the transducer downwards to remove all the air (Pictures 4 and 5). Refill the sheath with water. Continue to draw off as much air as possible and refill the sheath with water until you are sure that there is no air left in either the sheath or the water inlet.

5 Now that you have removed air bubbles that could interfere with the image, draw all the water out of the rubber sheath. (The transducer will be inserted into the patient without water in the sheath. After the transducer is inserted, water can be introduced again into the sheath.)

6 If a biopsy channel bracket UA1257 is being used, cover the transducer (and the rubber sheath) with a sterile condom containing a small amount of sterile imaging gel.

7 Now click the biopsy channel bracket onto the transducer.

8 Finally, cover the transducer plus the biopsy channel bracket with a second sterile condom containing a small amount of sterile imaging gel.

NOTE: *When the transducer is not being used for puncture and biopsy, the dummy channel bracket UA1272 must be in place. Cover the transducer plus UA1272 with a standard condom containing a small amount of imaging gel.*

Before you start imaging, the patient may require a small enema to clean the rectum as fecal material may disturb the ultrasound image.

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WARNING

We do not recommend use of the water standoff facility when the UA1257 biopsy channel bracket is in place and biopsies are to be performed. This is due to the strong likelihood of puncturing the rubber sheath with the biopsy needle. Instead, prior to performing the biopsy, the standoff should be drained of water.

WARNING

Do not use excessive force during insertion. Do not make excessive lateral movements during or after insertion. Risk of injury or tissue damage to the patient could occur under certain circumstances. A digital palpation of the rectum may need to be carried out by a clinician prior to insertion or use of the probe as a precautionary measure.

Puncture and Biopsy Facilities

Puncture and biopsy are possible with 8808. The appropriate puncture attachments are illustrated in the following pages with a brief description of their uses and operating instructions.

For transperineal puncture, puncture attachment UA1232 is available.

For transrectal puncture, a biopsy guide UA1257 is available in different versions. Whenever UA1257 is mentioned throughout this user guide, it refers to each of the UA1257 biopsy guides listed in the Product Data sheet.

The puncture equipment is illustrated in the following pages with a brief description of its use and operating instructions.

WARNING

It is essential for the patient's safety that only the correct puncture attachments, as described in this guide, are used. Never use unauthorized ombinations of transducers and puncture attachments or other manufacturers' puncture attachments.

For Transrectal Puncture

The UA1257 biopsy channel brackets are intended for transrectal puncture and biopsy. The transducer has an "open channel" into which one of these channel brackets can be fitted when the dummy channel bracket has been removed (see Figure 3).

UA1257 is available for different needle sizes and comes in both non-sterile reusable versions (light green) and in sterile-packed single-use versions (dark green) UA1257-S14 and UA1257S17E. Each version includes needle guide, biopsy channel bracket and clamp. Full product specifications for the puncture equipment can be found in the Product Data sheet that accompanies this user guide.

All needle guides for the UA1257 biopsy channel bracket are angled at 17.7° to the transducer's axis. The puncture line for UA1257 is shown in Figure 10.

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The transducer is prepared for transrectal puncture or biopsy by pulling a sterile transducer cover over the transducer, placing the appropriate needle guide in the UA1257 channel bracket (see Figure 5 and Figure 6) and clipping the channel bracket onto the transducer (See "Mounting a Transrectal Puncture Guide" on page 13.).

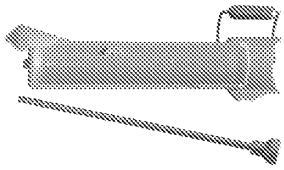


Figure 5. Biopsy channel bracket and needle guide before assembly.

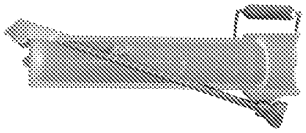


Figure 6. Biopsy channel bracket with the needle guide in place.

Non-sterile Reusable Biopsy Guides

The reusable versions of the UA1257 biopsy guide - which consist of UA1257-R17, UA1257-R17E and UA1257-R14 biopsy guides - are non-sterile when supplied and must be disinfected by immersion in a suitable solution and autoclaved.

The biopsy channel bracket may be damaged during use or processing, so it must be checked before use for cracks or irregularities in the surface. It should also be checked thoroughly once a month following the procedure in *Care, Cleaning & Safety*.

Sterile Single-use Biopsy Guides

The sterile single-use versions of the biopsy guide UA1257 come assembled in a peel pack. Contents are only sterile if the package is intact.

WARNING

Disposable components are packaged sterile and are intended for single-use only.

Do not use if:

- Integrity of packaging is violated.
- Expiration date has passed.
- Package label is missing.

The sterile-packed biopsy guides must be stored at a temperature range from +15 °C (+57 °F) to +25 °C (+77 °F) and at a storage humidity of 30% to 80%.

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WARNING

Sterile-packed components must be stored in a safe environment and kept out of direct sunlight. Large temperature changes during storage may cause condensation and violate the integrity of the packaging.

Please refer to *Care, Cleaning and Safety* for an example of how to open a sterile-packed product.

WARNING

For contaminated disposals such as transducer covers or needle guides, follow disposal control policies established for your office, department or hospital.

Mounting a Transrectal Puncture Guide

To mount a channel bracket and needle guide on the transducer:

1. If a dummy channel bracket is mounted on the transducer, remove it.
2. Pull a sterile transducer cover or a standard condom containing a suitable amount of sterile imaging gel over the transducer.
3. Slide the needle guide into the biopsy channel bracket as shown in Figure 6.
4. Insert the assembled needle guide and channel bracket into the open channel on the transducer. A small nodule on the end of the channel bracket fits into an indentation in the channel on the transducer to help you place the channel bracket correctly. Click the channel bracket into position on the transducer and lock it into place (see Figure 7).



Figure 7. Biopsy channel bracket UA1257 mounted on the transducer (here shown without condom).

5. After you attach the channel bracket, pull a sterile transducer cover containing a small amount of sterile imaging gel over the entire assembly (transducer plus biopsy channel bracket).
6. The needle can then be inserted into the needle guide. The Product Data sheet details the needle gauge suitable for the different needle guides

WARNING

Ensure that the channel bracket and needle guide are correctly positioned. Never insert the needle guide while the transducer is inside the patient.

To remove the channel bracket, remove the outer condom, open the lock and lift the channel bracket off the transducer.

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For Transperineal Puncture

The UA1232 metal puncture attachment (see Figure 8) is designed for transperineal puncture and biopsy. When UA1232 is being used, the dummy channel bracket UA1272 (shown in Figure 3) must be in place.

UA1232 consists of a needle guide and a mounting ring with a lock screw. The needle guide comprises 9 parallel guide channels, spaced 5 mm apart, each with an internal diameter of 2.1 mm, suitable for a 14-gauge needle. The guide is parallel to the centerline of the transducer.

Note: *The needle guide can be adjusted 70 mm lengthwise with respect to the mounting ring, using the adjustment screw.*

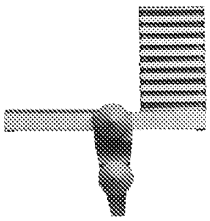


Figure 8. Puncture attachment UA1232.

Mounting the Transperineal Puncture Guide

To mount the transperineal puncture attachment, loosen the lock screw and slide the attachment over the tip of the transducer until the lock screw pressure-pad meets the steel stud on the side of the transducer. The puncture attachment should be correctly positioned (see Figure 9) before the lock screw is tightened. No force should be used when attaching the puncture attachment to the transducer

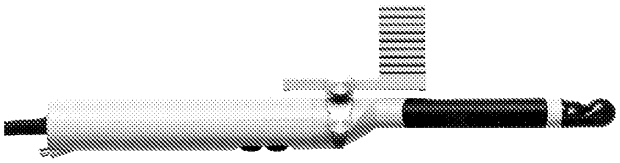


Figure 9. Puncture attachment UA1232 mounted on the transducer.

The puncture lines for UA1232 are shown in Figure 11.

All parts of the puncture attachment can be autoclaved or disinfected by immersion in a suitable solution.

⚠ **Caution:** When monitoring the image of the needle in the transverse plane during transperineal biopsy, the needle tip may at first appear as a weak echo and nearer to the transducer surface than it actually is. Continue to advance the needle until the brightest echo is achieved. This represents the correct position. The appearance of a weak echo is due to the fact that the transverse plane in practice has a certain 'thickness', and is at an angle of 15 degrees to the axis of the transducer.

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Caution: Always use the longitudinal plane image to check that the needle has advanced to the correct position. If you use the transverse plane, remember that the image plane's distance from the needle guide increases by 2.6mm for every 10mm distance from the transducer (see Figure 11). You must take this into account when using the transverse plane to determine the outline or structure of an organ.

Performing Puncture and Biopsy

WARNING

It is essential for the patient's safety that only the correct puncture attachments, as described in this guide, are used. Never use unauthorized combinations of transducers and puncture attachments or other manufacturers puncture attachments.

Before beginning a puncture or biopsy procedure, always check that the type number of the transducer and the type number or description of the puncture attachment match exactly those displayed on the system monitor.

WARNING

The puncture line on the image is an indication of the expected needle path. The needle tip echo should be monitored at all times so any deviation from the desired path can be corrected.

If not sterilized, cover the transducer with a sterile transducer cover.

If the transducer cover is damaged when attaching the puncture attachment, replace it with a new cover.

See the Product Data sheet for a list of available transducer covers.

Superimpose puncture line

Press the system **Puncture** or **Biopsy** control button to superimpose a puncture line on the image.

The puncture line will differ depending on the imaging plane orientation. In the sagittal plane, the puncture path is indicated by a line of dots. The distance between each puncture dot is 5mm.

In the transverse plane, a single dot indicates the point at which the needle will transect the imaging plane.

For transrectal puncture with biopsy channel bracket UA1257, the distance from the end of the needle guide to the first puncture dot on the imaging plane rotation axis is 79mm (see Figure 10).

If more than one puncture line is available, refer to the applicable system user guide for instructions on how to change which one appears.

Move the transducer until the puncture line transects the target. Insert the needle and monitor it as it moves along the puncture line to the target. The needle tip echo will be seen as a bright dot on the screen.

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WARNING

If the needle guide is detached from the transducer during interventional procedures, cover the transducer with a new transducer cover.

If the cover is damaged during interventional procedures, follow the policies of the hospital or clinic for treatment of the patient under such circumstances.

To remove the puncture line from the image, refer to the applicable system user guide for instructions.

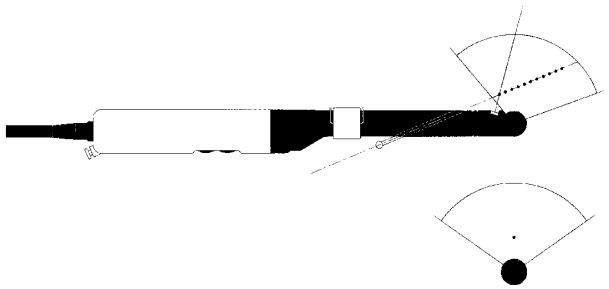


Figure 10. Illustration of the puncture line for biopsy channel bracket UA1257.

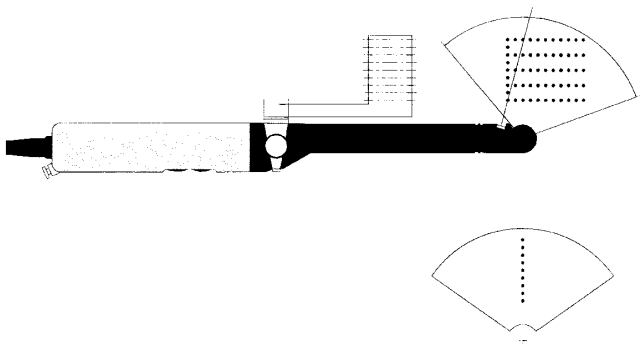


Figure 11. Illustration of the puncture lines for puncture attachment UA1232.

WARNING

When performing a biopsy, always make sure that the needle is fully drawn back inside the needle guide before moving the transducer.

Cleaning after Puncture and Biopsy

If biological materials are allowed to dry on the transducer, disinfection and sterilization processes may not be effective. Therefore, you must clean transducers immediately after use.

Use a suitable brush to make sure that biological material and gel are removed from all channels and grooves. See *Care, Cleaning & Safety* for cleaning instructions.

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Caution: Do not stick anything into the water inlet to clean it. Poking something into this hole can damage the water channel inside the transducer. You can clean the water channel by flushing it with water soon after use, before any foreign matter such as imaging gel has a chance to harden.

WARNING

For contaminated disposals such as transducer covers or needle guides, follow disposal control policies established for your office, department or hospital.

3D Imaging

3D imaging with the 8808 may be carried out in either of two ways:

- Freehand – where the transducer is combined with the appropriate 3D system software.
- Using mover support – where the transducer is combined with the appropriate 3D system software, the Magnetic Wheel Mover UA0513 and the Variable Friction Arm UA0553.

Magnetic Wheel Mover UA0513

Further information about the Magnetic Wheel Mover UA0513 can be found in the user guide for the Magnetic Wheel Mover.

Variable Friction Support Arm UA0553

Further information about the Variable Friction Support Arm UA0553 can be found in the user guide for the Variable Friction Support Arm.

Disposal

When the transducer is scrapped at the end of its life, national rules for the relevant material in each individual land must be followed. Within the EU, when you discard the transducer, you must send it to appropriate facilities for recovery and recycling. See the applicable system user guide for further details.

WARNING

For contaminated disposals such as transducer covers or needle guides, follow disposal control policies established for your office, department or hospital.

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LEGAL MANUFACTURER : BK Medical ApS, Mileparken 34, 2730 Herlev, Denmark. Tel.: +45 44528100 Fax: +45 44528199 Email: info@bkmed.dk

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Ultrasound-Guided Biopsy

4

Judy U. Ahrar and Kamran Ahrar

Introduction

Ultrasound-guided biopsy has become an essential diagnostic technique in radiology [1]. It is safe and accurate and is often used for confirmation of suspected malignancy and characterization of other lesions throughout the body. Initially, ultrasound-guided biopsies were restricted to large, superficial cystic lesions. Improvements in imaging technology and biopsy techniques now allow even small masses located deep within the body to be imaged and targeted for sampling under ultrasound guidance. This chapter outlines the equipment, advantages, disadvantages, applications, and techniques used in ultrasound-guided biopsies.

Equipment

Any ultrasonography unit that can image and localize a lesion within the body can also be used to guide a biopsy of that lesion. In general, the transducer that is most suitable for imaging of the organ of interest is also used to guide the biopsy. High-frequency linear transducers are appropriate for targeting more superficial lesions (Fig. 4.1),whereas low-frequency curved array transducers are more appropriate for targeting lesions that are located deep within the body (Fig. 4.2) (e.g., liver tumors). Needle-guidance systems are available for use with various ultrasonography units and transducers. The guidance system consists of an adaptor that attaches directly to the transducer (Fig. 4.3). Once attached to the transducer, the predicted needle path is displayed on the screen. The depth and angle of needle insertion can be adjusted by choosing from the available predetermined choices. The adaptor has a groove or slot to allow passage of the biopsy needle. The needle should be held firmly in place to avoid deviation from the predetermined path. Therefore, different sizes of needle guides are available to be inserted into the groove or slot of the adaptor. The guidance system helps maintain the needle path in the plane of the ultrasound beam, simplifying ultrasound-guided biopsies. On the other hand, the inability to operate the transducer and the needle separately from one another takes away some of the flexibility of the freehand needle-insertion technique (Fig. 4.4).

Advantages

Ultrasonography is appealing as an image-guidance modality for several reasons. Ultrasonography is readily available, relatively inexpensive, and portable. It allows multiplanar imaging in any conventional or arbitrary plane. Unlike computed tomography (CT), ultrasonography does not use ionizing radiation. Most importantly, ultrasound guidance provides real-time visualization and monitoring of the needle tip as it is advanced into the skin, through the overlying soft tissues, and into the biopsy target. This visualization of the needle tip allows precise needle placement while avoiding damage to the nearby structures. Color flow Doppler imaging can help identify the vascular nature of the mass and the adjacent vascular structures (Fig. 4.1) [2, 3]. The imaging plane can be adjusted to exclude vessels from the path of the needle. Watching the needle tip during the sampling process in real time helps ensure that the needle tip does not extend outside the mass and that the biopsy is obtained from the lesion of interest (Fig. 4.5).

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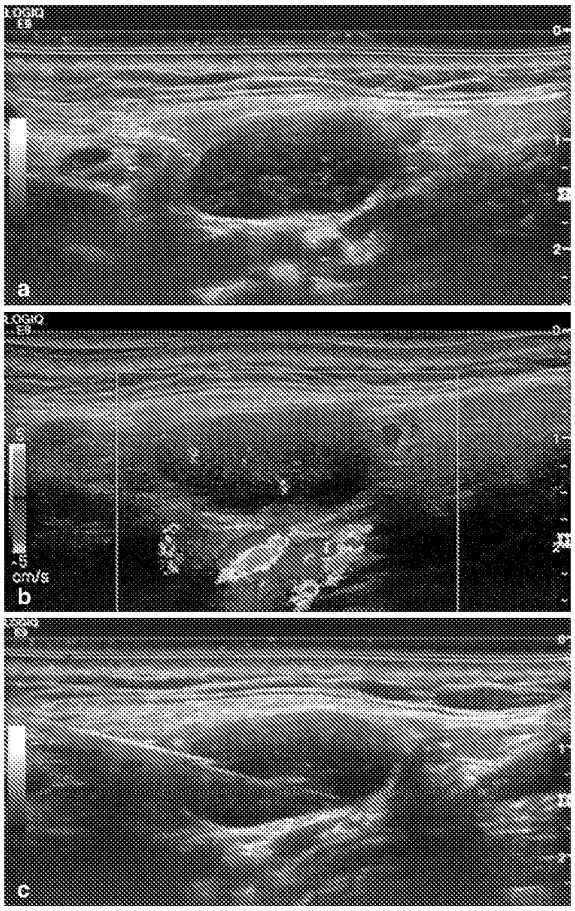


Fig. 4.1 A 51-year-old man with a history of lymphoma was referred for biopsy of an enlarged right cervical lymph node. A high-frequency (6–15 MHz) linear transducer was used to image this superficial lesion (**a**). Duplex Doppler sonography revealed some vascularity in the lesion and larger vascular structures deeper to the lesion (**b**). An 18-gauge core biopsy needle was used to obtain several core biopsy samples (**c**). A trajectory was chosen to obtain the longest possible core biopsy sample. Pathologic evaluation revealed mantle cell lymphoma, diffuse pattern

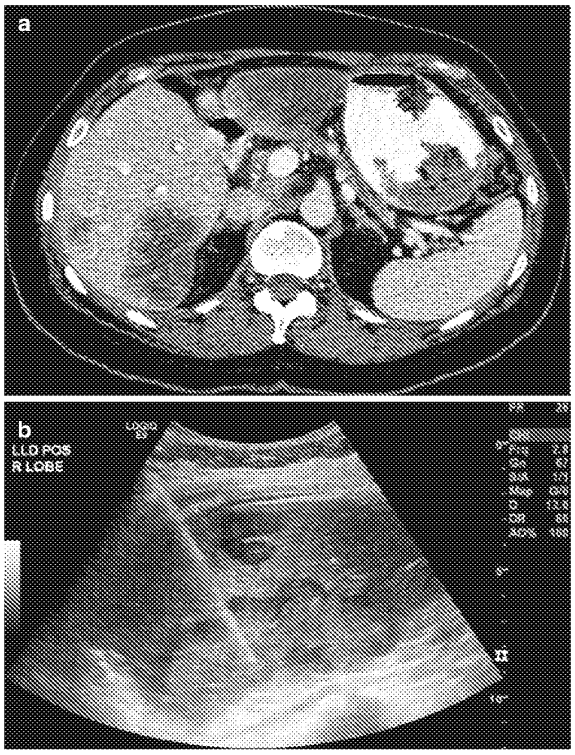


Fig. 4.2 A 68-year-old woman with a history of metastatic breast cancer was referred for a biopsy prior to enrollment in a clinical trial. An axial CT image of the liver (**a**) revealed a 6-cm mass in the medial aspect of segment VI. A smaller (2 cm) mass is seen more superficially closer to the liver capsule. With the patient in the left lateral decubitus position, real-time ultrasound guidance was used to target the medial lesion for sampling (**b**). When possible, the target liver lesion and biopsy path should be selected such that the needle traverses a segment of normal liver before entering the tumor. This may reduce the risk of bleeding and tumor seeding after the biopsy

Another major advantage of ultrasound guidance is that the patient can be placed in various positions and that steep out-of-axial-plane angles can be used for needle guidance. Flexibility in the positioning of the patient also adds to the patient's comfort during the biopsy. For example, the head of the bed may be elevated or the patient may be allowed to move slightly during the biopsy to get into a more comfortable position to relieve back or joint pain.

Compared to CT-guided biopsies, ultrasound-guided biopsies require less time to perform and can be more cost effective [4–6]. Some studies have suggested that ultrasound-guided biopsies are more accurate and have lower false-negative rates than CT-guided biopsies [6, 7].

Disadvantages

Not all lesions can be well visualized on ultrasonography. Ultrasound guidance is optimal for targeting lesions that are located superficially or at a moderate depth in a thin- to moderate-sized patient. Ultrasound guidance is of limited use in identifying and targeting lesions in obese patients or lesions located deep within the body. Similarly, ultrasound-guided biopsy may not be possible when lesions are located

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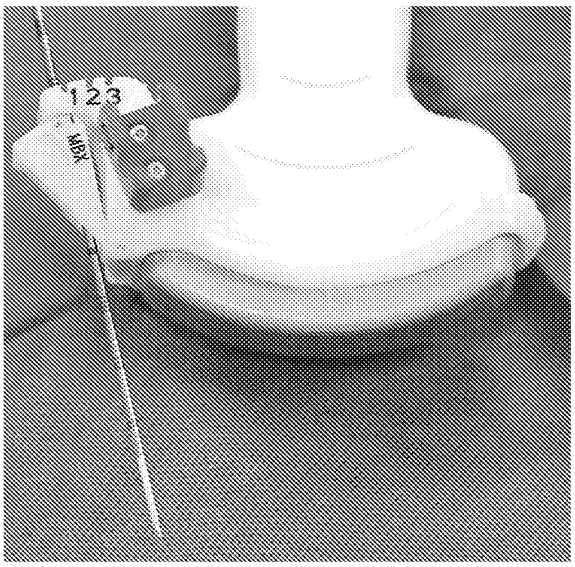


Fig. 4.3 In this photograph, the curved transducer is fitted with an adaptor with several predetermined angle settings. With this technique, the needle and the transducer work as a unit. The adaptor fits the needle and guides it to the target while preventing deviation of the needle from the set course

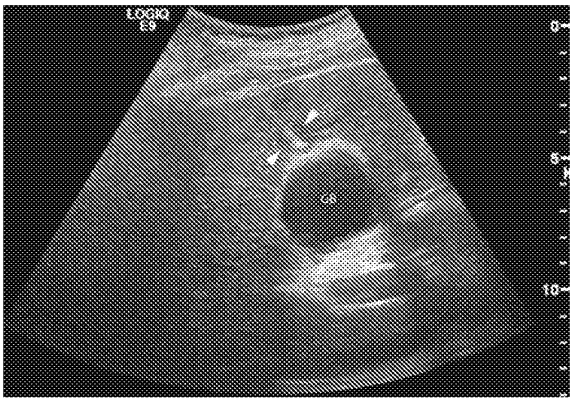


Fig. 4.5 A 54-year-old man with history of prostate cancer was referred for biopsy of a small liver lesion. Gray-scale sonographic image of the liver during the biopsy revealed a 1-cm hypoechoic tumor (*arrowheads*) adjacent to the gallbladder (*GB*). The echogenic needle is seen in the tumor. Real-time monitoring of the needle tip during fine-needle aspiration biopsy ensured safe, selective sampling of the small lesion without inadvertent puncture of the gallbladder

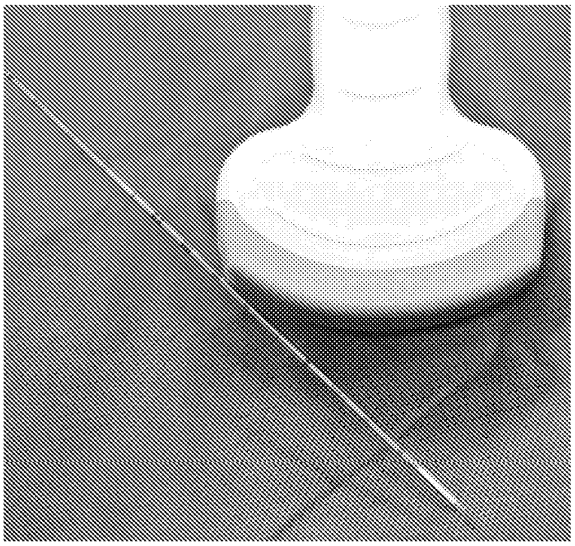


Fig. 4.4 In the "freehand technique," the needle and the transducer are operated separately from one another. The needle can be inserted at any angle. One can also choose an insertion site that is not directly in the imaging plane, but maintaining the needle tip in the imaging plane of the transducer is more challenging and requires experience

behind a reflective surface such as bone or gas-filled bowel and when the transducer cannot be positioned to look from a different angle.

Applications

Any mass that is well visualized on ultrasonography can be targeted for biopsy. This includes any superficial soft tissue mass, head and neck lesion, breast tumor, or solid or cystic mass in the liver, kidney, or spleen [8–14]. Ultrasound guidance is commonly used to perform liver biopsies. This may include biopsy of specific lesions within the liver or biopsy of liver parenchyma to investigate the cause and severity of liver failure. The left lobe of the liver can often be reached from an anterior subcostal approach. The sagittal imaging plane can be helpful for lesions closer to the dome of the liver, although a steep-angle approach may be necessary. Lesions in the inferior aspect of the right lobe of the liver may be approached by a lateral subcostal route. Frequently, lesions in the right lobe of the liver are approached through an intercostal route with the patient placed in left lateral decubitus or supine position. Ultrasound-guided biopsy of a renal mass can be performed if the patient is not morbidly obese and the kidney can be adequately imaged on ultrasonography (Fig. 4.6). Ultrasonography can also be used to guide core biopsies of native and transplanted renal parenchyma to determine the etiology of parenchymal disease. Other abdominal and retroperitoneal organs such as the pancreas and adrenal gland may

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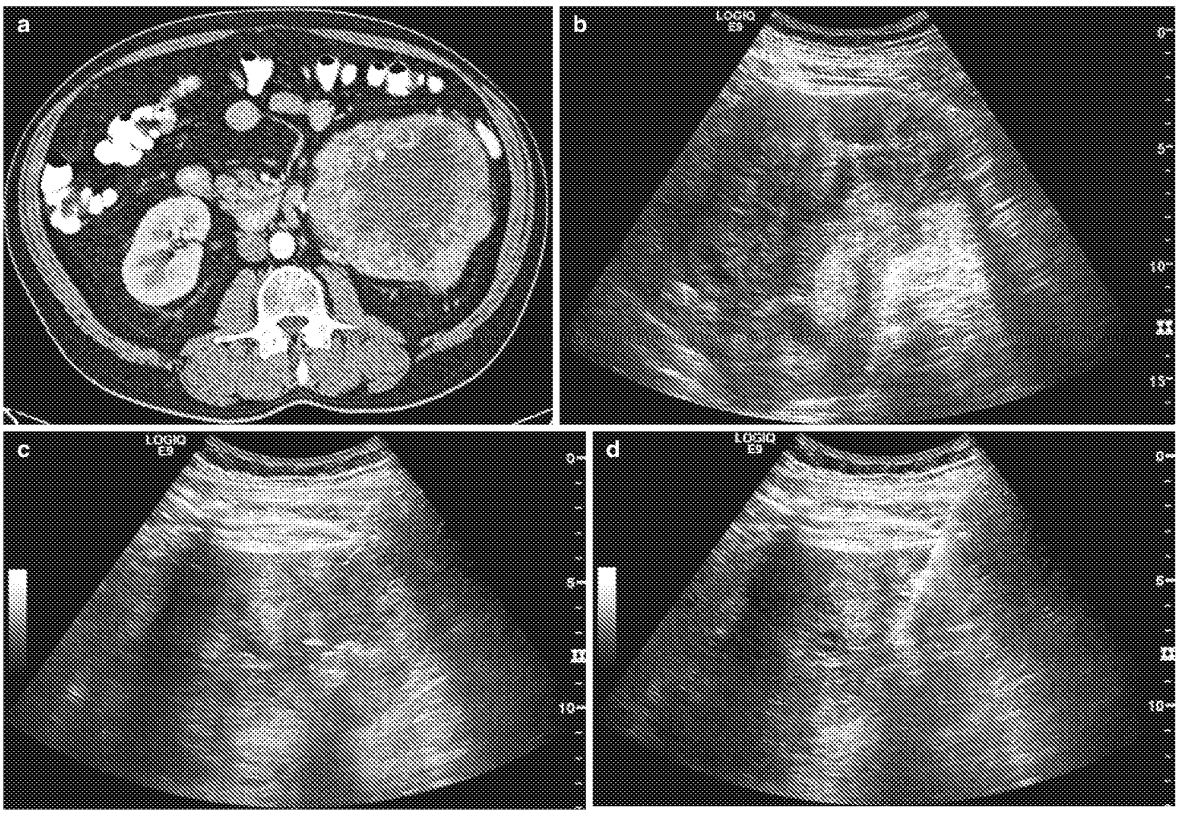


Fig. 4.6 An axial CT image of the abdomen (**a**) in a 53-year-old man revealed a large left renal mass with central necrosis. A gray-scale sonographic image (**b**) revealed a large mass with heterogeneous echogenicity. During ultrasound-guided biopsy (**c**), a 16-gauge guide needle is visualized with difficulty. When the stylet is replaced by the core biopsy needle, microbubbles introduced into the guide needle greatly enhance the echogenicity of the guide needle (**d**) and allow better visualization of the needle in the target

be targeted with ultrasound for biopsy [15, 16]. Ultrasound guidance can be used to biopsy lung, mediastinal, and pleural masses that abut the chest wall [17]. Some musculoskeletal lesions can be targeted using ultrasound guidance (Fig. 4.7) [18–20]. For retroperitoneal lesions, an anterior approach is preferred. Using specialized transducers, pelvic organs can be reached by transvaginal or transrectal approaches [21–23].

Techniques

Prior to ultrasound-guided biopsy, a limited ultrasound is performed to localize the lesion, select a suitable transducer, and plan the needle's path. The distance between the puncture site and the target is measured to help select an appropriate biopsy needle. In some practices, a sonographer is responsible for imaging the patient during the biopsy, while the physician advances the needle to the target. Experienced interventional radiologists do not require a sonographer's assistance, as the interventional radiologist will hold the transducer in one hand and the biopsy needle in the other hand. In this manner, hand-eye coordination is optimized.

Biopsy procedures are performed under sterile conditions. The transducer is covered with a sterile plastic cover. To prevent image degradation, ultrasound gel is placed inside the sterile cover to provide acoustic coupling. In addition, sterile gel is placed on the skin's surface. Others prefer to clean the transducer with alcohol and place it directly on the skin [24], and no increase in post-biopsy infection rates has been reported [25].

Ultrasound-guided biopsies are performed under continuous real-time visualization of the biopsy needle as it is advanced to the target. If a needle-guidance system is used,

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Fig. 4.7 An 11-year-old boy presented with pain and discomfort in the left thigh. Anteroposterior (**a**) and lateral (**b**) radiographs of the left femur revealed an expansile lesion of the distal femoral diaphysis, with osteoid matrix, suspicious for osteosarcoma. The radiographs do not reveal a significant soft tissue component. He was referred for image-guided biopsy. Transverse gray-scale ultrasound of the left femur (**c**) revealed a rind of soft tissue thickening, with a nodular component (*arrowhead*) with underlying cortical breakdown (*arrows*). The soft tissue component of the tumor was targeted for biopsy (**d**) using a 14-gauge semiautomatic core biopsy needle. Four samples were obtained. A pathologic review revealed high-grade osteoblastic osteosarcoma

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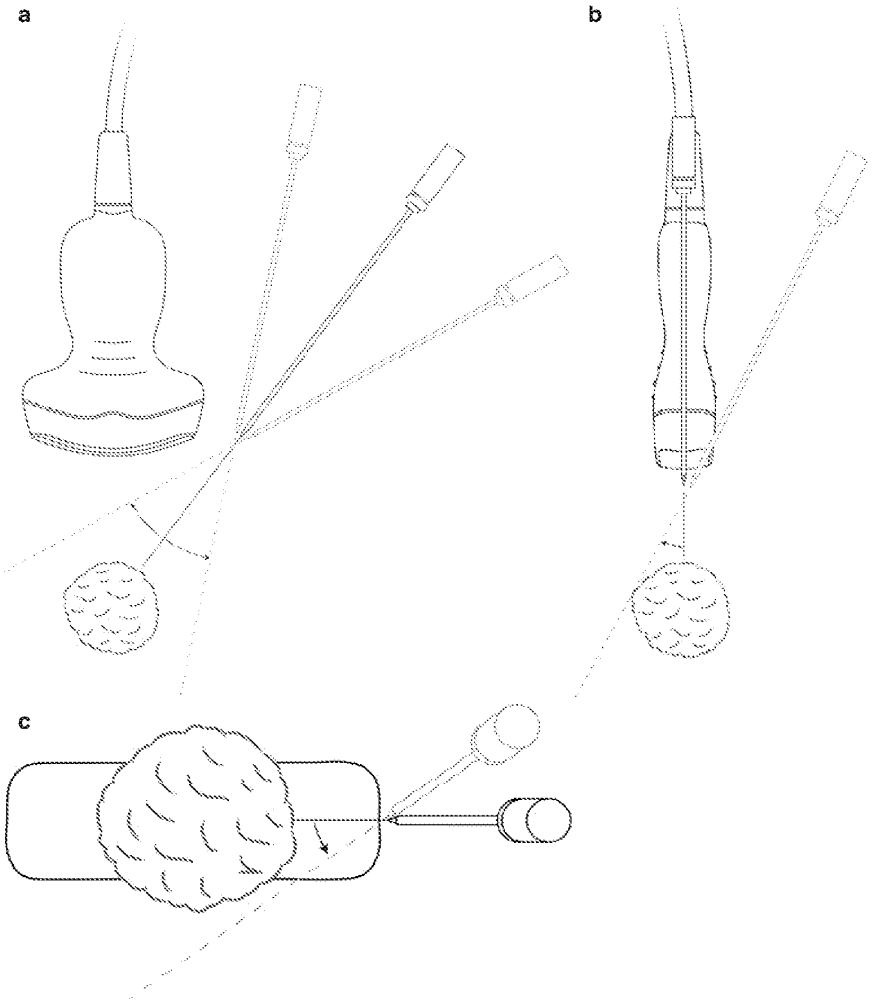


Fig. 4.8 Illustration of the freehand technique. (**a**) In this frontal view of the transducer, the target lesion and needle are in the imaging plane. The insertion angle is adjusted so that the needle penetrates the lesion. In the lateral (**b**) and superior (**c**) views, the artist demonstrates how the needle can deviate (*arrow*) from the imaging plane and potentially miss the target

a scanning plane is chosen so that the target lesion is lined up with the needle path. The depth of the needle insertion can be adjusted by choosing from the available predetermined angle choices. A needle guide of the correct size is attached or inserted into the transducer guide prior to insertion of the needle. The entire shaft of the needle can be constantly visualized when using a guidance system, making the needle-insertion process simple and efficient. It can be completed in one breath hold if needed. On the other hand, there is limited flexibility with the plane of imaging when using a rigid guidance system. Also, the needle must be placed close to the transducer and cannot be inserted at a more remote puncture site.

Experienced radiologists prefer to use a freehand technique without a needle guide [24, 26]. The operator holds the transducer in one hand and the needle in the other. With experience, one can use either hand as the needle or operating hand and avoid crossing hands, which may lead to difficulties in orientation. In this technique, the needle is freely inserted into the view of the transducer, providing great flexibility and allowing adjustments to be made during the biopsy. On the other hand, improper alignment of the needle tip and the plane of imaging (transducer) may lead to suboptimal visualization or nonvisualization of the needle tip (Fig. 4.8).

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Needle visualization may be enhanced by increasing the reflective or scattering properties of the biopsy needle [27–29]. This can be accomplished by dimpling or etching of the needle tip, using a screw-tip needle or coating the needle with Teflon or other reflective substances [30]. Jiggling the needle as it is advanced in the tissue, jiggling the stylet in and out of the needle, and keeping the bevel of the needle up may improve visualization of the needle [31]. Large-gauge needles cause brighter reflections and are more easily visualized than are small-gauge needles. Using the highest frequency possible improves visualization of the needle. Color flow Doppler imaging may also help visualize the needle tip [32, 33]. Needles are more difficult to visualize at shallow insertion angles [34]. When the needle is inserted nearly parallel to the ultrasound beam, the major portion of the ultrasound beam is reflected away from the transducer face, making it more difficult to visualize the needle. If the needle is inserted nearly perpendicular to the ultrasound beam, more of the beam is reflected back to the transducer face, allowing excellent needle visualization. Needles are more easily detected in fluid and tissues with low echogenicity than in highly echogenic tissues. Treated needles are most helpful in echogenic tissues.

A linear high-frequency transducer is optimal for targeting superficial lesions such as structures in the head and neck or superficial lymph nodes throughout the body (Fig. 4.1). A curved array transducer is often used to target lesions that are located at a moderate depth from the skin surface (Fig. 4.2). For example, lesions in the liver or kidney are often targeted using a curved array transducer (1- to 5-MHz). The ultrasound parameters should be optimized for visualization of the target lesion. The depth of the imaging is set to the depth of the lesion, and the focal zone is placed in the near field or just at the level of the lesion for better needle visualization. A single focal zone is preferred because multiple focal zones may decrease the frame rate.

Ideally, the interventional radiologist can visualize the needle and the target on the same image on the screen and can watch the needle as it is advanced toward the target. If the needle and the lesion are both visible on one image, but the angle of the needle is such that it would miss the target, the angle needs to be corrected (Fig. 4.8a). If the needle is already beyond the subcutaneous tissues, levering of the needle may not lead to the desired change in the angle of the trajectory. Oftentimes, the needle has to be withdrawn to just below the skin and reinserted at the desirable angle. When the needle deviates from the imaging plane, the tip will not be seen as it is advanced into the body (Fig. 4.8b, c). If not recognized, this may lead to injury of adjacent structures. First, the operator should visually inspect the relationship of the transducer and the needle on the patient. The transducer might have slipped on the skin and turned away from the puncture site. This can be easily corrected by realigning the transducer along the needle path. On the other hand, if the needle has deviated from the desirable imaging plane and is off target, the operator needs first to locate the needle tip by angling the transducer from side to side. Once the position of the needle tip relative to the target is determined (e.g., medial or cephalad), the needle is withdrawn and reinserted after slight correction toward the target (e.g., lateral or caudad). Occasionally, a firm mass located superficially in the subcutaneous tissues may be pushed out of the way by the needle tip. To secure the target, the operator can apply firm pressure, fixing the lesion in place while puncturing it with the biopsy needle. Also during biopsy of abdominal lesions, the operator may press the transducer firmly toward the lesion to reduce the skin-to-lesion distance and to displace any overlying loops of bowel [35]. Care must be taken to make sure the bowel loop is actually displaced out of the needle path and is not compressed between the transducer and the target.

In recent years, more sophisticated ultrasound units are fitted with software packages that allow fusion of previously obtained cross-sectional images with the real-time ultrasound examination (Fig. 4.9). This feature allows more confident sampling of the lesion and targeting of lesions that may be hard to visualize with ultrasound alone.

In summary, ultrasound guidance is an effective and efficient technique to target lesions or organs during biopsy procedures. Use of needle-guidance systems facilitates the procedure, but mastering the freehand technique allows the maximum flexibility during ultrasound-guided biopsies.

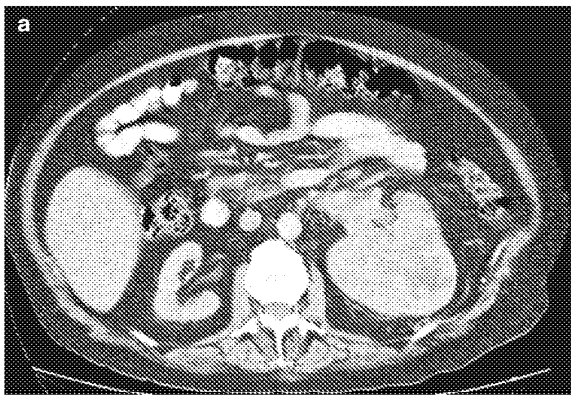


Fig. 4.9 An axial CT image of the abdomen (**a**) revealed a large ill-defined, infiltrative mass involving the lower pole of the left kidney. Ultrasound-guided biopsy was performed in the prone position (**b**) after fusion of the previously acquired CT images (*right*) with the real-time ultrasound image (*left*). The software allows real-time reconstruction of previously acquired CT images in any arbitrary plane, corresponding to that of the ultrasound transducer

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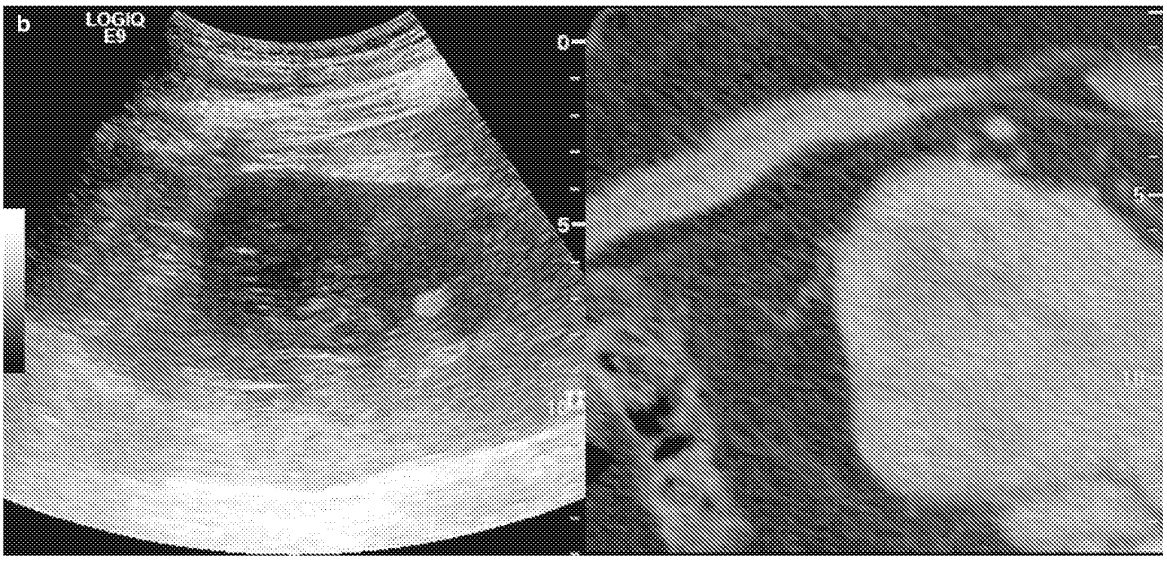


Fig. 4.9 (continued)

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District Court of The Hague
Corbin v Leapmed & Another
[case number]

WITNESS STATEMENT OF
SAHEED RASHID

I, **Saheed Rashid**, state as follows:

My relevant background

1. I am the Managing Director of a limited liability company established in the U.K called BXTAccelyon Limited (here: "BXTA"). BXTA is an established international specialist sales and distribution business in the field of prostate cancer, with a supply chain currently extending from the UK to New Zealand.

2. Since mid-2017, BXTA is the exclusive distributor, in a large number of countries, of the PrecisionPoint™ Transperineal Access System. This device is protected by EP 3 125 811 B1 (here: "the patent"). For The Netherlands, and for a large number of other countries, BXTA is the sole approved distributor of the PrecisionPoint™ device.

My instructions

3. I have been asked by Dutch counsel acting for Corbin to describe in general terms the steps taken by BXTA to commercialise the PrecisionPoint™ in both the U.K. and The Netherlands, and to say something about the way the markets have developed in those jurisdictions. I have also been asked to describe the impact the Surefire device, marketed by Leapmed and distributed in The Netherlands by Pelvitec, has had on sales of the PrecisionPoint™ device in The Netherlands.

4. I understand that this statement will be referred to by Corbin in Dutch preliminary injunction proceedings against Leapmed and its Dutch distributor Pelvitec. I confirm that the facts stated in this witness statement are within my own personal knowledge unless otherwise

stated, and are true to the best of my knowledge and belief. The opinions expressed herein are truly held.

The plan for a carefully controlled and well-supported roll-out of the PrecisionPoint™ device

5. I have been shown the Expert Report drawn up by Dr. Rick Popert, whom I have known for a number of years. Dr. Popert is one of the most eminent and well-respected consultant urologists in the UK.

6. As Dr. Popert explains in his report, the PrecisionPoint™ device allows for novel methods for performing transperineal ('TP') prostate biopsies under local anaesthetic ('LA'). As Dr. Popert explains, the device allows urologists to carry out systematic and targeted biopsies of the prostate easily, accurately and conveniently in an outpatient setting. The PrecisionPoint™ offers very significant clinical advantages compared both to conventional transrectal biopsy techniques, and to conventional transperineal techniques. Specifically, the PrecisionPoint™ enables safer and more accurate biopsies to be carried out in an outpatient setting, minimising the need to use expensive and limited operating theatre space.

7. Although the PrecisionPoint™ was FDA-approved at the time BXTA entered into a distribution agreement to distribute the device in mid-2017, the European registration for the device was not yet complete, and no sales of the device were possible until the CE certification had been obtained.

8. Introducing a new medical device presents unique challenges. For a successful launch of a new medical device, the relevant clinicians, who can occasionally be a little conservative in wanting to stick to their tried and tested ways of doing things, must be convinced that the new device offers a real and measurable improvements over what they were using before.

9. It is therefore necessary to have a well-respected peer explain clearly to them what the benefits of the device are, and to be able to do so on the basis of solid facts, backed up by his or her own clinical experience. Adequate training must be provided to ensure that the device continues to be used correctly, and mentoring must be made available, at least in the early stages of adoption, to assist in the migration to a new way of working, using the new tool. Ensuring patient welfare is, of course, paramount throughout the process.

10. BXTA had therefore devised a highly controlled plan for the roll-out of the PrecisionPoint™ device which required all healthcare professionals to attend training courses before any devices could be ordered. Support would also be provided by skilled clinical support staff, provided via BXTA until the urology teams were competent in the use of the PrecisionPoint™ device.

11. We recognized that although the procedure looked relatively straightforward, there were certain key skills that the healthcare professional would need to learn in order to become truly proficient, notwithstanding their experience in standard transrectal or transperineal grid-

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guided approaches. No devices would be supplied to hospitals or clinics unless the healthcare professionals working there had indeed followed the requisite training.

12. We set up the initial training courses with the assistance of Dr. Popert in August 2017 at Guys, in order to train clinicians ahead of the commercial release of the device which would take place only once CE certification had been achieved. A monthly training course was established at Guys with, initially, five or six consultants invited to learn the procedure from Dr Popert, who was still completing a number of clinical studies required to provide post-market surveillance for the FDA.

13. CE approval was granted in December 2017 and commercial sales commenced in January 2018, with the trained clinicians being supported in their first cases by Dr. Popert or one of his trained clinical team.

14. From January 2018, training courses were increased in attendee number to 10-12 delegates, and included international visitors. All of the first procedures in delegates' centres were supported by a clinical mentor. Local courses were started in New Zealand, Australia, Hong Kong, Singapore, Belgium and The Netherlands during the course of 2018.

15. Courses were expanded to include Clinical Nurse Specialists ('CNSs') in February 2019 and regular courses were established in Australia, New Zealand and The Netherlands. Courses in the UK were expanded to other cities including Bristol and Manchester. During the Covid pandemic, training courses were moved online as webinars across all regions from the UK to Australia.

16. Since August 2017, BXTA has conducted over 200 courses in over 14 countries and trained more than 2,000 clinicians and specialist nurses.

PrecisionPoint™ TRexit progress

17. Around 60,000 PrecisionPoint™ devices have been sold by BXTA since its launch in January 2018. There are now over 200 treatment centres using the device in 14 countries.

18. The UK average sales in the last 3 months indicate that 54% of all UK biopsies (approximately 60,000 biopsies annually) are now performed using the PrecisionPoint™ device. We expect full conversion to be achieved within two years.

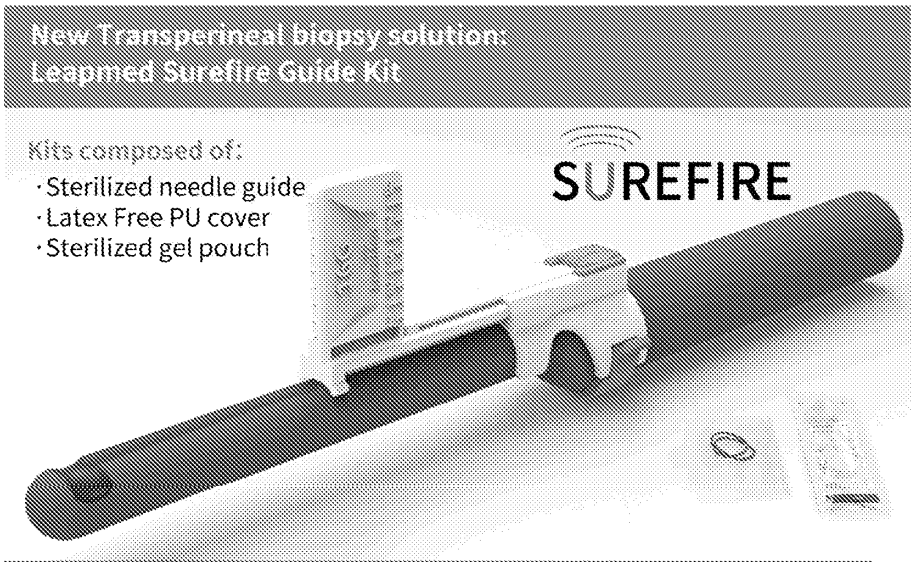
19. Australia and New Zealand are moving forward with their own versions of the TRexit initiative; approximately 21% of all Australasian biopsies are now carried out with the PrecisionPoint™ device.

The Leapmed Surefire device

20. Following the local market launch in late 2018, sales in The Netherlands were approaching 2,000 PrecisionPoint™ devices per year (around 5% of all biopsies) by the end of 2020.

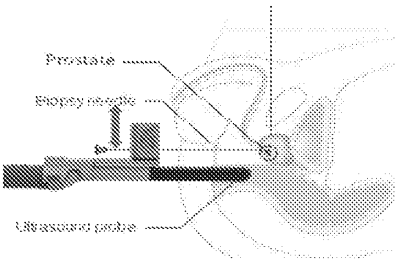
21. This was a healthy start, but unfortunately sales have since plummeted to virtually zero because of the promotion, by Pelvitec, of an adaptation of Leapmed's 'Surefire' device which turns it into something which resembles the PrecisionPoint™ device.

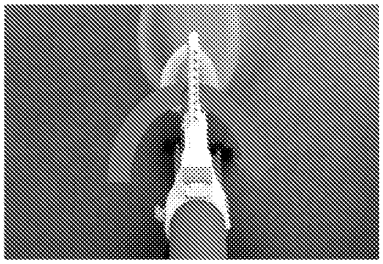
22. I attach the brochure for the Leapmed Surefire device to this witness statement as **Exhibit SR-1**. The following image is taken from the brochure:



23. The Surefire device was originally intended to be used in a similar way to conventional grid-guided transperineal biopsies. The vertical grey protrusion shown in the image above is in essence a "slice" of the grid typically used to collect biopsy cores in conventional transperineal biopsy procedures by making multiple perforations in the perineum. The biopsy needle is passed through the numbered grooves in order to make multiple perforations and take multiple cores. The device can then be rotated to allow further perforations to be made in other parts of the prostate. This process is illustrated in the brochure as follows:

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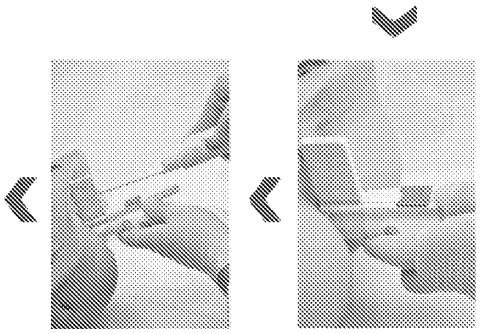
·Vertical adjustable: Up to 9 puncture holes ·Free Sectorial plane adjustment

24. As with conventional transperineal biopsy procedures, the making of a significant number of punctures in the perineum will require a general anaesthetic.

25. The modification advocated by the Dutch distributor involves the addition of a coaxial access needle to the Surefire device in one of the grooves of the grey protrusion, through which the biopsy needle can be inserted.

26. The addition of the coaxial access needle allows a biopsy needle to be inserted to take a biopsy sample, with subsequent repositioning of the probe / access needle combination *while the access needle remains in place*, so that the biopsy needle can then be reinserted, through the same perforation, to take a biopsy from a different area of the prostate. In this way, the number of punctures can be reduced to two, and an intervention is possible under local anaesthetic. This is exactly how the PrecisionPoint™ device works.

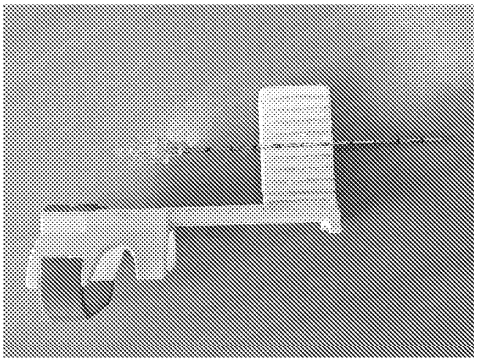
27. This modification (the addition of an access needle to the Surefire device) is not described in the Surefire brochure, and indeed this way of using the device is not described in the official instructions for use at all. I attach the English-language IFU for the Surefire as **Exhibit SR-2**. They confirm that in normal use, the biopsy needly is simply inserted through the grooves, with the probe being rotated to allow the needle to be inserted at targeted locations:



6.Rotate the probe to targeted locations. Insert biopsy needle through groove.

5.Unlock/lock button to adjust needle plate to proper position.

28. The modification (the addition of a coaxial access needle or "coaxial introducer needle") is described in additional information provided by the Dutch distributor, Pelvitec. I attach the instructions provided by Pelvitec to this witness statement as **Exhibit SR-3A** (the Dutch original language version) and **Exhibit SR-3B** (a highlighted version with an English translation of the relevant parts). This document, which bears a footer with Pelvitec's address, shows a photograph of a modified Surefire device with the coaxial access needle in place:



29. The biopsy needle (not shown in this image) then is passed through the coaxial access needle to take the biopsy cores.

30. The same document explains that the coaxial access needle shown in the photograph reproduced above is not present in the packaging for the Leapmed device. That is not

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surprising, since, as I note above, the use of a coaxial access needle is not contemplated in the instructions for use for the Leapmed device.

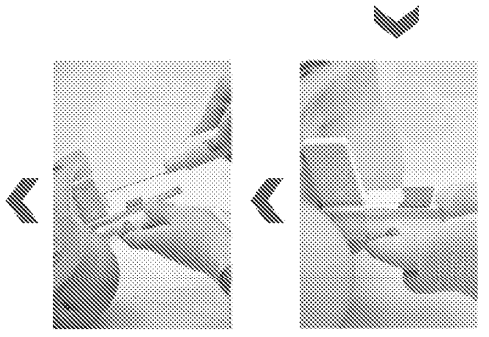
31. Pelvitec does however supply suitable access needles to allow the modification it advocates to be made. I attach a copy of email correspondence dated 4 June 2021 between a representative of Pelvitec, Mr. Hero Mulder, and a Dutch representative of BXTA, Mr Wilco van der Lugt as **Exhibit SR-4**.

32. Although I do not speak Dutch, it has been explained to me, and I believe, that this correspondence relates to the use of coaxial access needles, and that Mr. Mulder confirms, in his email, that the Surefire is almost always used in combination with a coaxial access needle (i.e. in a manner which is not in accordance with the IFU for the Surefire device).

33. Mr. Mulder goes on to state that Pelvitec can supply two different suitable coaxial needles. Mr. Mulder also notes that the Surefire is already used in a number of Dutch hospitals.

34. This is also the email in which Mr. Mulder provides Pelvitec's own protocol for using the Surefire. (This is **Exhibit SR-3A**, mentioned above). In these instructions, the clinician is instructed to use the same perforation in the skin for the taking of multiple biopsies, and to move the probe in the horizontal plane from left to right, *without rotation*.

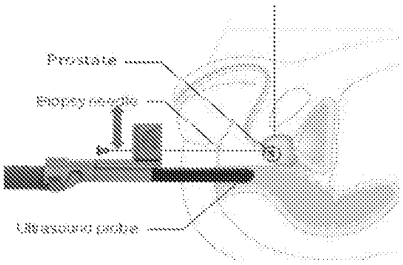
35. This is a significant deviation from the official instructions for use of the Surefire, which specifically instructs clinicians to rotate the device, the idea being that the vertical grid is thereby moved to the desired position, so that fresh punctures can be made, using the biopsy needle, through the desired groove, at the desired location. Here again is the relevant part of the official IFU, showing the probe being rotated to the targeted locations before the biopsy needle is inserted through the groove:



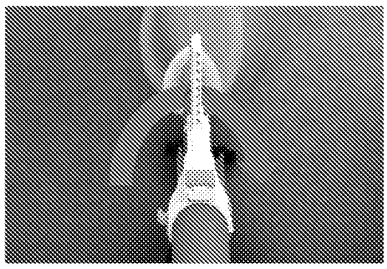
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36. The necessity to deviate from the official instructions for use is dictated by the presence of the coaxial access needle, which was not part of the original device or the original IFU, but which is an essential part of the modification proposed by Leapmed and Pelvitec.

37. It is clear that rotating the device in the manner indicated in the official instructions for use while a coaxial access needle is inserted would be impossible without causing trauma. Rotating the coaxial access needle would tear the area around the puncture in which the coaxial needle is embedded. The difficulty can perhaps best be appreciated when considering the following image from the original Surefire brochure:



· Vertical adjustable: Up to 9 puncture holes



· Free Sectorial plane adjustment

38. The adaptation of the Surefire device is also illustrated in Leapmed's instruction video[1]. This video, which shows the use of a biopsy needle through the coaxial introducer needle, is exhibited as **Exhibit SR-5**. A number of screen-grabs, accompanied by a transcript of the video, are exhibited as **Exhibit SR-6**.

39. The addition of the coaxial access needle allows the operator to use the Surefire device in a way it was not intended to be used, in order to obtain the same advantages as those provided by the PrecisionPoint™ device. In effect, the adaptation advocated by Pelvitec turns the Surefire into a poor man's PrecisionPoint™ device, capable of taking multiple biopsies from just two perforations.

40. The modified Surefire device is being targeted by its distributor, Pelvitec, specifically at hospitals in The Netherlands where clinicians have been trained by BXTA and by our regional experts to carry out transperineal prostate biopsies under local anaesthetic using the PrecisionPoint™ device.

41. In this way, Leapmed and Pelvitec are able to profit from the considerable investments made by BXTA in training clinicians in the use of the PrecisionPoint™ device. Leapmed sells its

[1] Presently available at: https://www.youtube.com/watch?v=TxjuS06J2Rs&feature=youtu.be

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device at a fraction of the price of the PrecisionPoint™ device. That is no doubt possible because Leapmed did not itself have to make any investments in developing and seeking regulatory approval for the the PrecisionPoint™ device, or in training physicians in how the device should be used: it was instead able to benefit directly from the investments Corbin and BXTA had already made.

42. I believe that unless Leapmed and Pelvitec are restrained as a matter of urgency, the Dutch market will effectively be a lost market for the PrecisionPoint™.

Statement of truth

43. The facts stated in this witness statement are true to the best of my knowledge and belief and the opinions stated herein are truly held. I am prepared to attend Court and confirm the contents of this witness statement under oath.

Signed: 

Saheed Rashid

This 15 October 2021

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List of Exhibits

SR-1 Brochure for the Leapmed Surefire device

SR-2 IFU for the Surefire

SR-3A Additional instructions of Pelvitec

SR-3B Highlighted version of Exhibit SR-3A

SR-4 E-mail correspondence between Wilco van der Lugt and Hero Mulder

SR-5 YouTube video: https://www.youtube.com/watch?v=TxjuS06J2Rs&feature=youtu.be

SR-6 Transcript and screen-grabs from SR-5

TRU-CUT®

Soft Tissue Biopsy Needles

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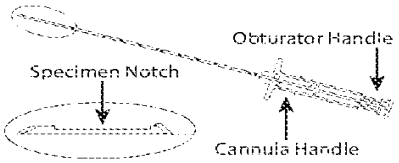
MERIT MEDICAL®

TRU-CUT®

English

Soft Tissue Biopsy Needles

INSTRUCTIONS FOR USE



INDICATIONS FOR USE:

Tru-Cut® Soft Tissue Biopsy Needle is a device that introduces a cannula into soft tissue such as breast, lungs, lymph nodes and prostate, etc. for diagnostic evaluation.

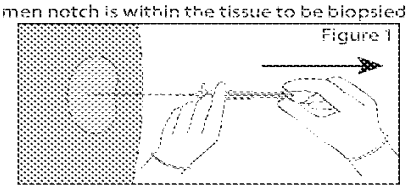
WARNING: This needle is not designed for puncturing the skin. Excessive force or resistance when the needle is extended may result in a bent specimen notch. A bent specimen notch will interfere with needle function and possibly cause tissue tearing. Excessive lateral force applied against the obturator handle of the needle may interfere with the function of the stop mechanism and may result in deeper tissue penetration than is desired with the potential for tissue or organ damage.

INSTRUCTIONS FOR USE:

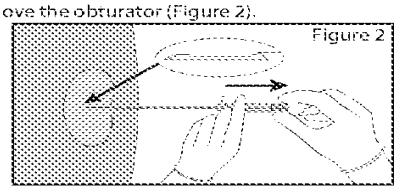
1. Using sterile technique, prepare the biopsy site.
2. Remove packaging. Remove protective sheath.
3. Test for proper function and alignment by sliding the cannula over the obturator several times. If the parts do not move easily, the unit should be discarded.

BIOPSY PROCEDURE (EXCEPT BREAST BIOPSY)

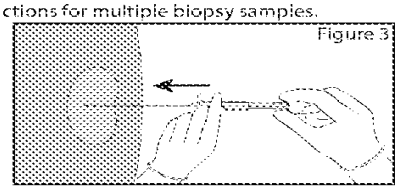
4. Retract the obturator to cover the specimen notch. Hold the cannula handle and insert the needle assembly so that the specimen notch is within the tissue to be biopsied (Figure 1).



5. Retract the cannula to expose the specimen notch. **Note:** Do not move the obturator (Figure 2).

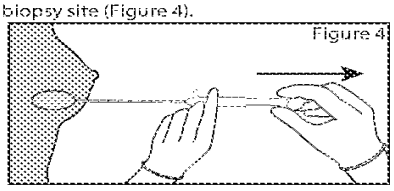


6. To cut the tissue, quickly advance the cannula handle (Figure 3). If another biopsy of the same tissue is required, leave the cannula positioned at the target biopsy site and follow instructions for multiple biopsy samples.

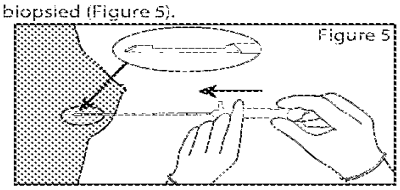


INSTRUCTIONS FOR THE BREAST BIOPSY

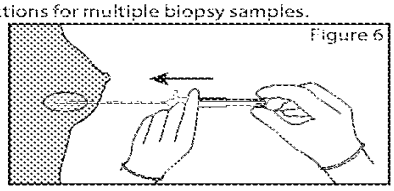
7. Retract the obturator to cover the specimen notch. Hold the cannula handle and insert the needle assembly to the edge of the biopsy site (Figure 4).



8. Hold cannula handle firmly. Quickly advance the obturator as far as permitted to position the specimen notch in the tissue to be biopsied (Figure 5).



9. To cut the tissue, quickly advance the cannula handle (Figure 6). If another biopsy of the same tissue is required, leave the cannula positioned at the target biopsy site and follow instructions for multiple biopsy samples.



FOR MULTIPLE BIOPSY SAMPLES

- Hold the cannula handle in a fixed position.
- Lift the obturator shaft slightly to clear the stop mechanism.
- Pull the obturator back to remove it from the cannula.
- Remove the sample from the specimen notch.
- To reinsert the obturator into the cannula, align the obturator shaft with the open side of the cannula handle and the specimen notch facing up. Slide the obturator forward until the obturator shaft locks into the handle.
- Follow one of the sampling procedures described to take additional biopsies.

10. Withdraw the needle assembly with the cannula still advanced over the obturator.
11. Advance the obturator to remove the biopsy specimen from the specimen notch.

WARNING:

- Not intended for use in bone.
- Do not use if package is damaged.

CAUTION: For single use only. Re-use may result in a non-functional product or contribute to cross contamination.

Only clinicians who have been properly trained in this procedure, including patient preparation, sample preservation and the use of image guidance for percutaneous biopsy, should use this device.

SYMBOL	DESIGNATION
	Use By: YYYY-MM-DD
LOT	Lot Number
REF	Catalog Number
STERILE R	Sterilized using Irradiation
	Do Not Use if Package is Damaged
	Single Use
℞ONLY	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician

Medical Device.

Sterile Package.

CORBIN_CLINICAL-001130

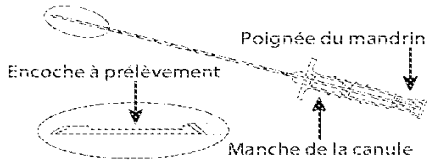
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TRU-CUT®

French

Aiguilles de biopsie pour tissus mous

MODE D'EMPLOI



MODE D'EMPLOI :

L'aiguille à biopsie des tissus mous Tru-Cut® est un dispositif qui introduit une canule dans les tissus mous tels que les seins, les poumons, les ganglions lymphatiques, la prostate, etc. à des fins d'évaluation diagnostique.

AVERTISSEMENT : Cette aiguille n'est pas conçue pour inciser la peau. Le mandrin peut se plier au niveau de l'encoche à prélèvement s'il est soumis à une force importante ou rencontre une résistance lorsqu'il est sorti de la canule. Une encoche à prélèvement tordue peut entraîner un mauvais fonctionnement de l'aiguille et une déchirure des tissus. Une force latérale importante appliquée sur la poignée du mandrin de l'aiguille peut modifier le mécanisme d'arrêt automatique et provoquer une pénétration des tissus plus profonde que prévue pouvant endommager les tissus ou l'organe concerné.

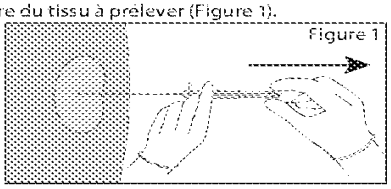
MODE D'EMPLOI :

1. En utilisant une technique stérile, préparer le champ opératoire.
2. Retirer l'emballage. Retirer la gaine de protection.
3. S'assurer du bon fonctionnement de l'aiguille en faisant glisser plusieurs fois la canule sur le mandrin. N'utiliser l'aiguille à biopsie que si les deux parties coulissent parfaitement.

PROCÉDURE DE BIOPSIE (SAUF BIOPSIE DU SEIN)

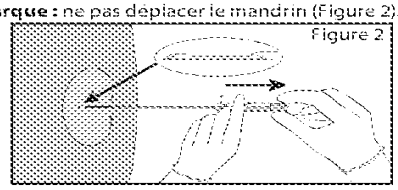
4. Rétracter le mandrin pour recouvrir l'encoche à prélèvement. Tenir le manche de la canule et introduire l'aiguille jusqu'à la bordure du tissu à prélever (Figure 1).

Figure 1



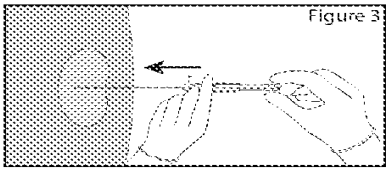
5. Rétracter la canule pour découvrir l'encoche à prélèvement. **Remarque :** ne pas déplacer le mandrin (Figure 2).

Figure 2



6. Pour sectionner le tissu, repousser rapidement vers l'avant le manche de la canule (Figure 3). Si une biopsie de tissus est nécessaire, laisser la canule en place au niveau du site de biopsie ciblé et suivre les instructions pour biopsies multiples.

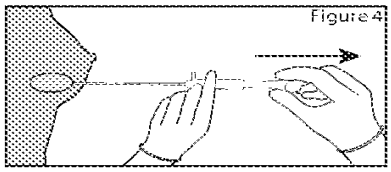
Figure 3



TECHNIQUE POUR BIOPSIE DU SEIN

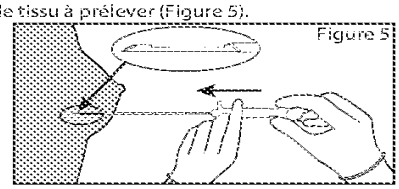
7. Rétracter le mandrin pour recouvrir l'encoche à prélèvement. Tenir le manche de la canule et introduire l'aiguille jusqu'à la bordure du tissu à prélever (Figure 4).

Figure 4



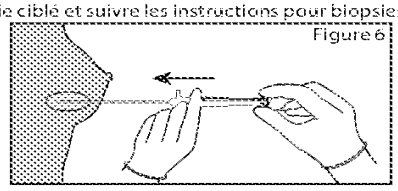
8. Maintenir fermement le manche de la canule. Pousser le mandrin à fond d'un geste rapide : l'encoche se trouve ainsi dans le tissu à prélever (Figure 5).

Figure 5



9. Pour sectionner le tissu, repousser rapidement vers l'avant le manche de la canule (Figure 6). Si une autre biopsie de tissus est nécessaire, laisser la canule en place au niveau du site de biopsie ciblé et suivre les instructions pour biopsies multiples.

Figure 6



TECHNIQUE POUR BIOPSIES MULTIPLES

- Maintenir le manche de la canule en position fixe.
- Soulever légèrement la poignée du mandrin pour la dégager du mécanisme automatique.
- Sortir le mandrin dans la canule.
- Retirer le prélèvement de l'encoche.
- Introduire le mandrin dans la canule. Positionner la poignée du mandrin dans la partie ouverte du manche de la canule. Pousser la poignée jusqu'à enclenchement du mécanisme d'arrêt automatique.
- Pour d'autres biopsies, suivre l'une des techniques de prélèvement proposées.

10. Retirer l'aiguille en la maintenant dans la position où l'encoche du mandrin est recouverte par la canule.
11. Pousser le mandrin pour retirer l'échantillon prélevé.

AVERTISSEMENT :

- Non conçue pour les os.
- Ne pas utiliser si l'emballage est endommagé.

MISE EN GARDE : Usage unique seulement. Une réutilisation peut provoquer le mauvais fonctionnement du produit ou contribuer à une contamination croisée.

Seuls des cliniciens correctement formés à cette procédure, y compris à la préparation du patient, à la préservation d'échantillon et à l'utilisation du guidage par imagerie pour la biopsie percutanée devraient utiliser ce dispositif.

SYMBOLE	DÉSIGNATION
	Date limite d'utilisation : AAAA-MM-JJ
LOT	Numéro de lot
REF	Numéro de référence
STERILE R	Stérilisé par irradiation
	Ne pas utiliser si l'emballage est endommagé
	Usage unique
℞ONLY	Mise en garde : La législation fédérale des États-Unis stipule que ce produit ne doit être vendu que par ou sur ordonnance d'un médecin

Dispositif médical.

Emballage stérile.

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TRU-CUT®

Italian

Aghi per biopsia dei tessuti molli

ISTRUZIONI PER L'USO



INDICAZIONI PER L'USO:
L'ago per biopsia dei tessuti molli Tru-Cut® è un dispositivo che introduce una cannula in tessuti molli come mammella, polmoni, linfonodi, prostata, ecc. per la valutazione diagnostica.

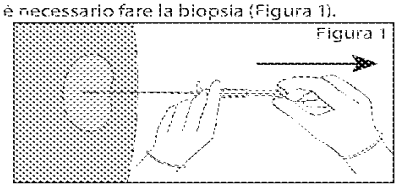
AVVERTENZA: questo ago non è concepito per forare la pelle. Una forza eccessiva o resistenza quando l'ago è esteso può risolversi con una vaschetta di prelievo piegata. Una vaschetta di prelievo piegata interferirà con il funzionamento dell'ago e probabilmente causerà il taglio del tessuto. Una eccessiva forza laterale applicata contro il manico dell'otturatore dell'ago può interferire con il funzionamento del meccanismo di arresto e può provocare una penetrazione nel tessuto più profonda di quanto voluto con il rischio di danni al tessuto o all'organo.

INSTRUZIONI PER L'USO:

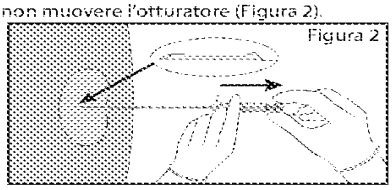
1. Usando una tecnica sterile, preparare il punto per la biopsia.
2. Rimuovere la confezione. Rimuovere l'involucro protettivo.
3. Fare un test per il corretto funzionamento ed allineamento facendo scorrere la cannula sull'otturatore varie volte. Se le parti non si muovono facilmente, l'unità deve essere scartata.

PROCEDURA DI BIOPSIA (ECCETTO BIOPSIA DEL SENO)

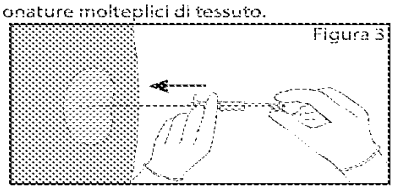
4. Ritirare l'otturatore per coprire la vaschetta di prelievo. enere il punto centrale della cannula e inserire l'assemblaggio con l'ago in modo che la vaschetta di prelievo sia dentro il tessuto di cui è necessario fare la biopsia (Figura 1).



5. Ritirare la cannula per esporre la vaschetta di prelievo.
Nota: non muovere l'otturatore (Figura 2).

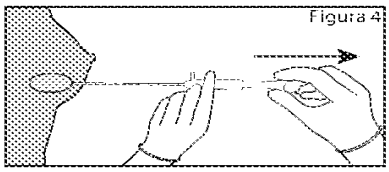


6. Per tagliare il tessuto, far avanzare velocemente l'impugnatura della cannula (Figura 3). Se è richiesta un'altra biopsia dello stesso tessuto, lasciare la cannula posizionata al punto di biopsia prefissato e seguire le istruzioni per le campionature molteplici di tessuto.

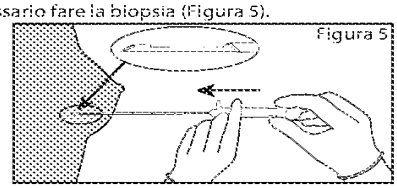


ISTRUZIONI PER LA BIOPSIA DEL SENO

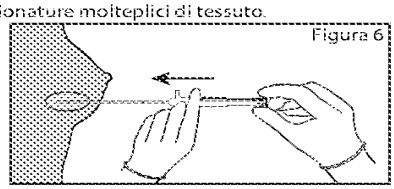
7. Ritirare l'otturatore per coprire la vaschetta di prelievo. Tenere il punto centrale della cannula e inserire l'assemblaggio dell'ago al margine del punto di biopsia (Figura 4).



8. Tenere saldamente il manico della cannula. Far avanzare velocemente l'otturatore per quanto è possibile per posizionare la vaschetta di prelievo nel tessuto di cui è necessario fare la biopsia (Figura 5).



9. Per tagliare il tessuto, far avanzare velocemente l'impugnatura della cannula (Figura 6). Se è richiesta un'altra biopsia dello stesso tessuto, lasciare la cannula posizionata al punto di biopsia prefissato e seguire le istruzioni per le campionature molteplici di tessuto.



PER CAMPIONI MULTIPLI DI BIOPSIA

- Tenere il manico della cannula in una posizione fissa.
- Alzare leggermente l'asse dell'otturatore per liberare il sistema di arresto.
- Tirare indietro l'otturatore per rimuoverlo dalla cannula.
- Rimuovere il campione dalla vaschetta di prelievo.
- Per inserire di nuovo l'otturatore nella cannula, allineare l'asse dell'otturatore con la parte aperta del manico della cannula e con la vaschetta di prelievo di fronte. Far scorrere l'otturatore in avanti finché l'asse dell'otturatore si aggancia al manico.
- Seguire una delle procedure di campionatura descritte per effettuare biopsie ulteriori.

10. Ritirare l'assemblaggio dell'ago con la cannula ancora sopra l'otturatore.
11. Far avanzare l'otturatore per rimuovere il campione della biopsia dalla vaschetta di prelievo.

AVVERTENZA:

- Non utilizzare sull'osso.
- Non usare se la confezione è danneggiata.

ATTENZIONE: esclusivamente monouso. Il riutilizzo può rendere non funzionale il prodotto o contribuire alla contaminazione crociata. Questo dispositivo deve essere utilizzato esclusivamente da medici specializzati nella relativa procedura, la quale comprende la preparazione del paziente, la salvaguardia del campione e l'impiego di una guida a immagine per biopsia percutanea.

SIMBOLO	DESIGNAZIONE
	Data di scadenza: AAAA-MM-GG
LOT	Numero di lotto
REF	Numero di catalogo
STERILE R	Sterilizzato tramite irraggiamento
	Non utilizzare se la confezione è danneggiata
2	Monouso
℞ ONLY	Attenzione: la legge federale (USA) limita la vendita di questo dispositivo ai soli medici o dietro prescrizione medica.

Dispositivo medico.

Confezione sterile

CORBIN_CLINICAL-001132

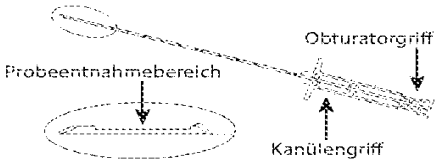
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TRU-CUT®

German

Weichteilgewebe-Biopsienadeln

GEBRAUCHSANWEISUNG



INDIKATIONEN FÜR DIE VERWENDUNG:
Die Tru-Cut® Weichteilgewebe-Biopsienadel ist ein Gerät, das eine Kanüle in Weichteilgewebe wie Brust, Lunge, Lymphknoten und Prostata usw. zur diagnostischen Beurteilung einführt.

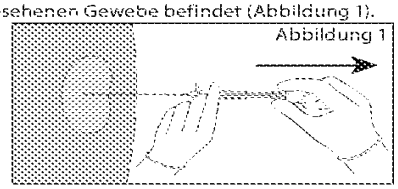
ACHTUNG: Diese Nadel ist nicht zur Punktierung der Haut geeignet. Stärkere Krafteinwirkung oder Widerstand gegen den Obturator, während dieser aus der stützenden Außenkanüle ausgefahren ist, kann dazu führen, dass sich der Obturator am Probeentnahmebereich verbiegt. Ein verbogener Probeentnahmebereich stört die Funktionstüchtigkeit des Stop-Mechanismus der Nadel und kann zu tieferer Penetration als gewünscht führen mit der Gefahr der Gewebe- oder Organschädigung.

GEBRAUCHSANWEISUNG:

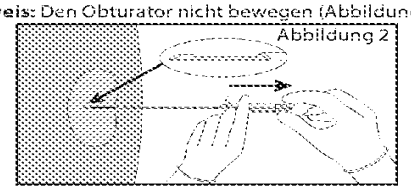
1. Zur Vorbereitung der Biopsie, die Einstichstelle nach üblichen sterilen Techniken vorbereiten.
2. Verpackung entfernen. Nadelschutz entfernen.
3. Vor Benutzung der Nadel, die ordnungsgemäße Funktion und Ausrichtung durch mehrmaliges Verschieben der Kanüle über den Obturator überprüfen. Wenn sich die Teile nicht leicht bewegen lassen, sollte die Nadel verworfen werden.

ANWENDUNG BEI GEWÖHNLICHER BIOPSIE (AUSSER BRUSTBIOPSIE)

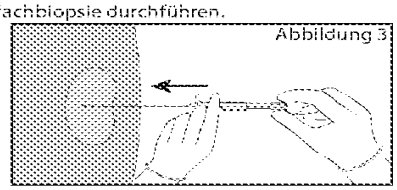
4. Der Obturator muß völlig zurückgeschoben sein, damit der Probeentnahmebereich überdeckt ist. Am Kanülenansatz halten, und die Nadel so einführen, dass der Probeentnahmebereich sich in dem für die Biopsie vorgesehenen Gewebe befindet (Abbildung 1).



5. Die Kanüle am größeren Kanülengriff herausziehen, um den Gewebeprobebereich für das Gewebe freizumachen. **Hinweis:** Den Obturator nicht bewegen (Abbildung 2).

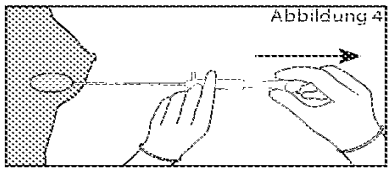


6. Zum Abtrennen von Gewebe den Kanülengriff schnell vorwärts bewegen (Abbildung 3). Falls eine weitere Biopsie vom gleichen Gewebe erforderlich ist, die Kanüle in der gleichen Position belassen und die Schritte für eine Mehrfachbiopsie durchführen.

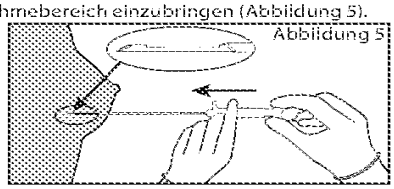


ANWENDUNG BEI DER BRUSTBIOPSIE

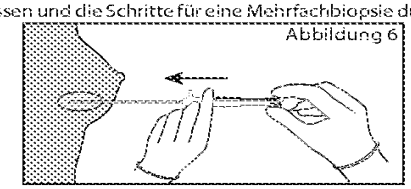
7. Der Obturator muß völlig zurückgeschoben sein, damit der Probeentnahmebereich überdeckt ist. Am Kanülenansatz halten, und die Nadel bis zu dem Gewebe einführen, aus dem die Probe entnommen werden soll (Abbildung 4).



8. Den größeren Kanülengriff stabil halten. Den Obturator rasch soweit wie möglich vorschieben, um das Gewebe in den Entnahmebereich einzubringen (Abbildung 5).



9. Zum Abtrennen von Gewebe den Kanülengriff schnell vorwärts bewegen (Abbildung 6). Falls eine weitere Biopsie vom gleichen Gewebe erforderlich ist, die Kanüle in der gleichen Position belassen und die Schritte für eine Mehrfachbiopsie durchführen.



MEHRFACHBIOPSIE

- Die Kanüle in der richtigen Position halten.
- Den Obturator am Schaft leicht anheben, um den Stopmechanismus zu öffnen.
- Den Obturator zurückziehen und aus der Kanüle entfernen.
- Die Probe aus dem Entnahmebereich entfernen.
- Um den Obturator wieder in die Kanüle einzuführen, den Obturatorschaft mit der offenen Seite der Kanüle ausrichten und den Gebeweentnahmebereich einführen. Den Obturator weiter vorschieben, bis der Schaft in den Stop-Mechanismus einrastet.
- Zur weiteren Gewebeentnahme eines der beschriebenen Entnahmebeispiele befolgen.

10. Die gesamte Nadel herausziehen, wobei die Kanüle über den Obturator geschoben bleibt.
11. Den Obturator nach vorne schieben, um die Gewebeprobe aus dem Probeentnahmebereich zu entfernen.

ACHTUNG:

- Nicht geeignet für den Einsatz in Knochen.
- Nicht verwenden, wenn die Verpackung beschädigt ist.

ACHTUNG: Nur zum Einmalgebrauch. Eine Wiederverwendung kann zu dazu führen, dass das Produkt keinen Gebrauchswert hat. Sie kann auch zu Kreuzkontamination beitragen.

Dieses Gerät sollte nur von Klinikern, die für dieses Verfahren einschliesslich der Vorbereitung des Patienten, der Aufbewahrung der Proben und der Verwendung von Bildanleitungen zur perkutanen Biopsie geschult wurden, verwendet werden.

SYMBOL	ERKLÄRUNG
	Verfalisdatum: JJJJ-MM-TT
LOT	Chargennummer
REF	Katalognummer
STERILE R	Durch Bestrahlung sterilisiert
	Nicht verwenden, wenn Packung beschädigt ist
	Einmalgebrauch
℞ONLY	Vorsicht: Nach US-amerikanischem Bundesrecht darf dieses Gerät nur von einem Arzt oder auf eine ärztliche Anordnung hin abgegeben werden.

Medizinisches Gerät.

Sterile Verpackung.

CORBIN_CLINICAL-001133

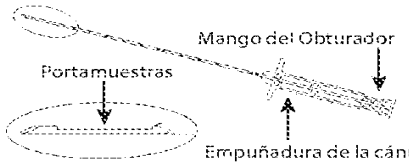
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TRU-CUT®

Spanish

Agujas para biopsia de tejido blando

INSTRUCCIONES DE USO



INDICACIONES DE USO:

La aguja para biopsia de tejido blando Tru-Cut® es un dispositivo que introduce una cánula en tejido blando como mamas, pulmones, nódulos linfáticos, próstata, etc. para su evaluación diagnóstica.

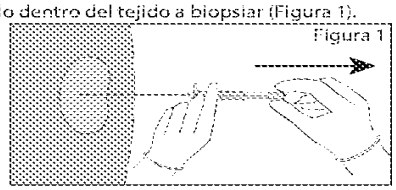
ADVERTENCIA: Esta aguja no está diseñada para penetrar la piel. Una fuerza o resistencia excesiva cuando la aguja es extendida puede causar que el espacio portamuestras se doble. Un espacio portamuestras doblado interferirá en el funcionamiento de la aguja y podrá rasgar el tejido. Una excesiva fuerza lateral aplicada sobre la empuñadura del obturador puede interferir con el mecanismo de freno de este y provocar una penetración en el tejido más profunda de la deseada con el consiguiente daño potencial en el órgano o tejido.

INSTRUCCIONES DE USO:

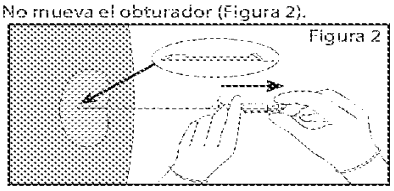
1. Utilizando una técnica estéril, prepare el punto de biopsia.
2. Retire el envase. Retire la vaina protectora.
3. Compruebe el correcto funcionamiento y alineación deslizando la cánula sobre el obturador varias veces. Si las partes no se mueven fácilmente, la unidad debe ser desechada.

PROCEDIMIENTO DE BIOPSIA (EXCEPTO PARA BIOPSIA DE MAMA)

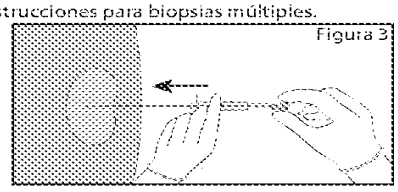
4. Retraiga el obturador para cubrir el espacio portamuestras. Sujete la empuñadura de la cánula e introduzca el conjunto de la aguja de forma que el espacio portamuestras esté situado dentro del tejido a biopsiar (Figura 1).



5. Retraiga la cánula para exponer el espacio portamuestras. **Nota:** No mueva el obturador (Figura 2).

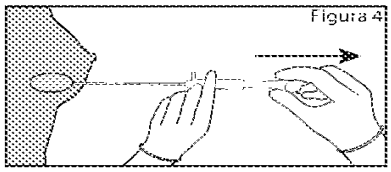


6. Para cortar el tejido, avance rápidamente la empuñadura de la cánula (Figura 3). Si se necesita otra biopsia del mismo tejido, deje la cánula posicionada en el sitio de biopsia y siga las instrucciones para biopsias múltiples.

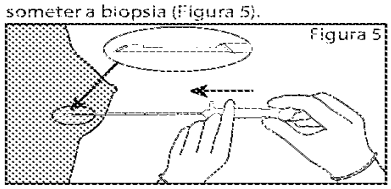


INSTRUCCIONES DE USO EN BIOPSIAS DE MAMA

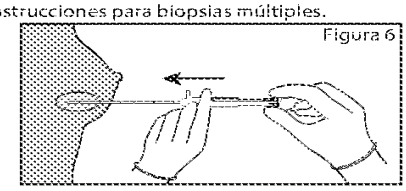
7. Retraiga el obturador de forma que cubra el espacio portamuestras. Sujete la empuñadura de la cánula e inserte el ensamblaje de la aguja hasta el borde del punto de biopsia (Figura 4).



8. Sujete firmemente la empuñadura de la cánula. Avance rápidamente el obturador todo lo que pueda de manera que el espacio portamuestras se encuentre dentro del tejido que se va a someter a biopsia (Figura 5).



9. Para cortar el tejido, avance rápidamente la empuñadura de la cánula (Figura 6). Si se necesita otra biopsia del mismo tejido, deje la cánula posicionada en el sitio de biopsia y siga las instrucciones para biopsias múltiples.



PARA LA OBTENCIÓN DE MUESTRAS MÚLTIPLES

- Sujete la empuñadura de la cánula en la posición fijada.
- Levante ligeramente el mango del obturador para librar el mecanismo de freno.
- Tire del obturador para extraerlo de la cánula.
- Extraiga la muestra del espacio portamuestras.
- Para volver a insertar el obturador dentro de la cánula, sitúe el mango del obturador alineado con el lado abierto de la empuñadura de la cánula y el espacio portamuestras hacia arriba. Deslice el obturador hacia delante hasta que el mango de éste quede bloqueado en la empuñadura de la cánula.
- Siga uno de los dos procedimientos de recolección de muestras descritos para obtener biopsias adicionales.

10. Retire el conjunto de la aguja con la cánula que permanece avanzada sobre el obturador.
11. Avance el obturador para extraer la muestra del espacio portamuestras.

ADVERTENCIA:

- No indicada para ser usada sobre tejido óseo.
- No utilizar si el paquete está dañado.

PRECAUCIÓN: utilizarse solo una vez. Volver a utilizarlo podría dar por resultado un producto no funcional o contribuir con la contaminación cruzada.

Solo deben usar este dispositivo los médicos que han recibido la capacitación adecuada en este procedimiento, incluida la preparación del paciente, la conservación de las muestras y el uso de una guía de imágenes para la biopsia percutánea.

SÍMBOLO	DESIGNACIÓN
	Fecha de vencimiento: DD-MM-AAAA
LOT	Número de lote
REF	Número de catálogo
STERILE R	Esterilizado por radiación
	No utilizar si el envase está dañado
	Para un solo uso
℞ ONLY	Precaución: La legislación federal de los Estados Unidos solo autoriza la venta de este dispositivo a través de un médico o por orden de este.

Dispositivo médico.

Paquete estéril.

CORBIN_CLINICAL-001134

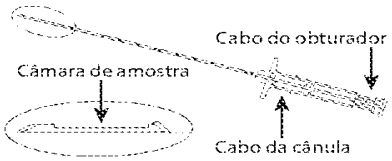
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TRU-CUT®

Portuguese

Agulhas para Biópsia de Tecido Mole

INSTRUÇÕES DE UTILIZAÇÃO



INDICAÇÕES DE UTILIZAÇÃO:

A Agulha para Biópsia de Tecido Mole Tru-Cut® é um dispositivo que introduz uma cânula nos tecidos moles, por exemplo, mama, pulmões, gânglios linfáticos e próstata, etc., para avaliação de diagnóstico.

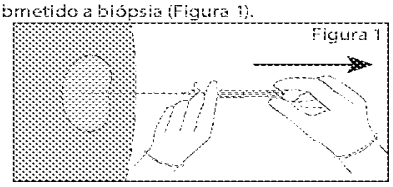
AVISO: Esta agulha não se destina à punção da pele. A força ou resistência excessiva sobre a agulha extendida pode resultar na torção da câmara de amostra. A câmara de amostra torcida interferirá com a função da agulha e provocará possivelmente rotura do tecido. A força lateral excessiva aplicada contra o cabo do obturador da agulha pode interferir com a função do mecanismo de paragem e pode resultar numa penetração tecidular mais profunda que o desejado, com potencial dano do tecido ou orgão.

INSTRUÇÕES DE UTILIZAÇÃO:

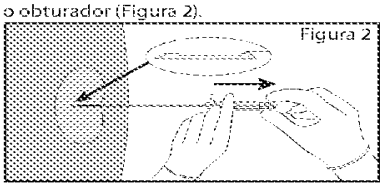
1. Utilizando tecnica estéril, preparar o local de biópsia. Segurar o cabo da cânula e inserir o conjunto da agulha de modo a que a câmara de amostra esteja dentro do tecido a ser submetido a biópsia
2. Retirar a embalagem. Retirar o revestimento de protecção.
3. Testar função e alinhamento adequado deslizando a cânula sobre o obturador diversas vezes. A unidade deverá ser eliminada, se as partes não se moverem facilmente.

PROCEDIMENTO DE BIÓPSIA (EXCEPTO BIÓPSIA DA MAMA)

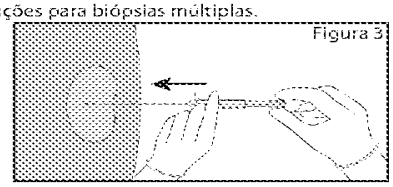
4. Recolher o obturador para tapar a câmara de amostra. Segurar o cabo da cânula e inserir o conjunto da agulha de modo a que a câmara de amostra esteja dentro do tecido a ser submetido a biópsia (Figura 1).



5. Recuar a cânula para expôr a câmara de amostra. **Nota:** Não mover o obturador (Figura 2).

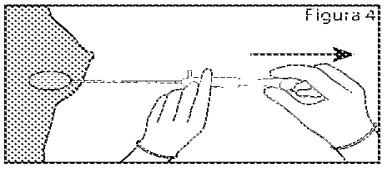


6. Para cortar o tecido, avançar rápidamente o cabo da cânula (Figura 3). Se fôr necessária outra biópsia do mesmo tecido, deixar a cânula posicionada no local de biópsia e seguir as instruções para biópsias múltiplas.

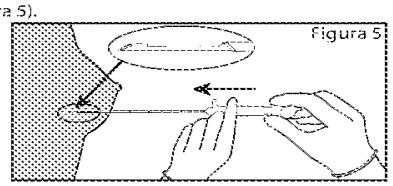


INSTRUÇÕES PARA A BIÓPSIA DA MAMA

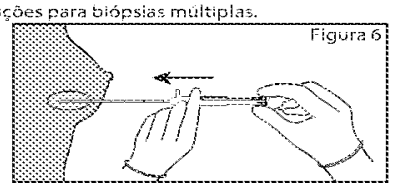
7. Recolher o obturador para tapar a câmara de amostra. Segurar o cabo da cânula e inserir o conjunto da agulha no corte do local de biópsia (Figura 4).



8. Segurar firmemente o cabo da cânula. Avançar rápidamente o obturador, o máximo possivel, de forma a colocar a câmara de amostra dentro do tecido a ser submetido a biópsia (Figura 5).



9. Para cortar o tecido, avançar rápidamente o cabo da cânula (Figura 6). Se fôr necessária outra biópsia do mesmo tecido, deixar a cânula posicionada no local de biópsia e seguir as instruções para biópsias múltiplas.



PARA AMOSTRAS MÚLTIPLAS DE BIÓPSIA

- Segurar o cabo da cânula numa posição fixa.
- Levantar ligeiramente o cabo do obturador para desobstruir o mecanismo de paragem.
- Puxar o obturador para o retirar da cânula.
- Retirar a amostra da câmara de amostra.
- Para re-inserir o obturador no interior da cânula, alinhar o cabo do obturador com o lado aberto do cabo da cânula e a câmara de amostra coincidentes. Deslizar o obturador para diante até que o cabo do obturador bloqueie no interior do cabo da cânula.
- Seguir um dos procedimentos de amostragem descritos para realizar biópsias adicionais.

10. Retirar o conjunto da agulha, com a cânula ainda sobre o obturador.
11. Avançar o obturador para retirar a amostra de biópsia da câmara de amostra.

AVISO:

- Não deve ser usada em osso.
- Não utilizar se a embalagem estiver danificada.

ATENÇÃO: apenas para uma única utilização. A reutilização poderá resultar num produto não funcional e contribuir para a contaminação cruzada.

Apenas médicos com formação adequada para este procedimento, incluindo preparação do doente, preservação de amostras e utilização de orientação por imagiologia para biópsia percutânea, deverão utilizar este dispositivo.

SÍMBOLO	DESIGNAÇÃO
	Prazo de validade: AAAA-MM-DD
LOT	Número de lote
REF	Número de catálogo
STERILE R	Esterilizado através de irradiação
	Não utilizar caso a embalagem esteja danificada
	Utilização única
℞ONLY	Atenção: A lei federal (EUA) restringe a venda deste dispositivo por ou segundo a prescrição de um clínico

Dispositivo Médico.

Embalagem esterilizada.

CORBIN_CLINICAL-001135

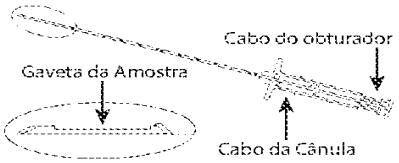
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TRU-CUT®

Portuguese-Brazil

Agulhas para biópsia de tecidos moles

INSTRUÇÕES DE USO



INDICAÇÕES DE USO:

A agulha para biópsia para tecidos moles Tru-Cut® é um dispositivo que introduz uma cânula no tecido mole, como mama, pulmão, linfonódulos e próstata, etc., para avaliação de diagnóstico.

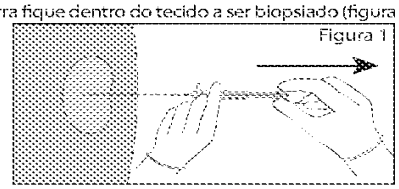
AVISO: Esta agulha não é projetada para punção da pele. Força ou resistência excessivas quando a agulha estiver estendida pode entortar a gaveta da amostra. Uma gaveta da amostra torta irá interferir na função da agulha e possivelmente causar ruptura do tecido. força lateral excessiva contra o cabo do obturador da agulha pode interferir na função do mecanismo de parada e pode resultar em uma penetração do tecido mais profunda do que o desejado, com potencial de causar dano ao tecido ou ao órgão.

INSTRUÇÕES DE USO:

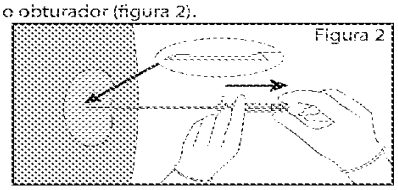
1. Usando uma técnica estéril, prepare o local da biópsia.
2. Remova a embalagem. Remova o estojo protetor.
3. Teste quanto ao funcionamento e alinhamento adequados deslizando a cânula sobre o obturador várias vezes. Se as peças não se moverem facilmente, a unidade deve ser descartada.

PROCEDIMENTO DA BIÓPSIA (EXCETO BIÓPSIA DE MAMA)

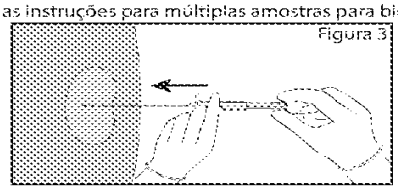
4. Retraia o obturador para cobrir a gaveta da amostra. Segure o cabo da cânula e insira o conjunto da agulha de forma que a gaveta da amostra fique dentro do tecido a ser biopsiado (figura 1).



5. Retraia a cânula para expor a gaveta da amostra. **Nota:** Não mova o obturador (figura 2).

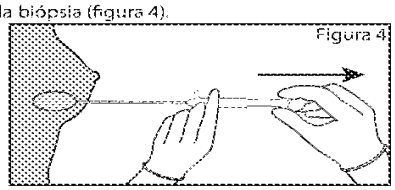


6. Para cortar o tecido, avance rapidamente o cabo da cânula (figura 3). Se uma outra biópsia do mesmo tecido for necessária, deixe a cânula posicionada no local alvo da biópsia e siga as instruções para múltiplas amostras para biópsia.

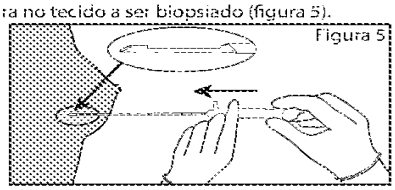


INSTRUÇÕES PARA BIÓPSIA DE MAMA

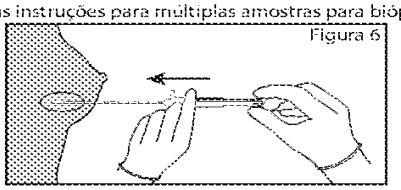
7. Retraia o obturador para cobrir a gaveta da amostra. Segure o cabo da cânula e insira o conjunto da agulha até a borda do local da biópsia (figura 4).



8. Segure firmemente o cabo da cânula. Avance rapidamente o obturador o máximo possível para posicionar a gaveta da amostra no tecido a ser biopsiado (figura 5).



9. Para cortar o tecido, avance rapidamente o cabo da cânula (figura 6). Se uma outra biópsia do mesmo tecido for necessária, deixe a cânula posicionada no local alvo da biópsia e siga as instruções para múltiplas amostras para biópsia.



PARA MÚLTIPLAS AMOSTRAS PARA BIÓPSIA

- Segure o cabo da cânula em uma posição fixa.
- Levante o eixo do obturador ligeiramente para liberar o mecanismo de parada.
- Puxe de volta o obturador para removê-lo da cânula.
- Retire a amostra da gaveta da amostra.
- Para reinserir o obturador na cânula, alinhe o eixo do obturador com o lado aberto do cabo da cânula e a gaveta da amostra virado para cima. Deslize o obturador para frente até que o eixo do obturador trave dentro do cabo.
- Siga um dos procedimentos de amostragem descritos para obter biópsias adicionais.

10. Retire o conjunto da agulha com a cânula ainda avançada sobre o obturador.
11. Avance o obturador para retirar a amostra para biópsia da gaveta da amostra.

AVISO:

- Não se destina a uso nos ossos.
- Não use se a embalagem estiver danificada.

ATENÇÃO: Somente para uso único. O reuso pode levar a um produto não funcional ou contribuir para contaminação cruzada.

Somente médicos adequadamente treinados neste procedimento, incluindo preparação de paciente, preservação de amostra e uso de imagem guia para biópsia percutânea, devem usar este dispositivo.

SÍMBOLO	DESIGNAÇÃO
	Usar antes de: AAAA-MM-DD
LOT	Número do lote
REF	Número de catálogo
STERILE R	Esterilizado por irradiação
	Não use se a embalagem estiver danificada
	Uso único
℞ONLY	Atenção: Leis federais dos EUA determinam que este dispositivo só pode ser vendido por médicos ou sob prescrição médica

Dispositivo médico.

Pacote Estéril.

CORBIN_CLINICAL-001136

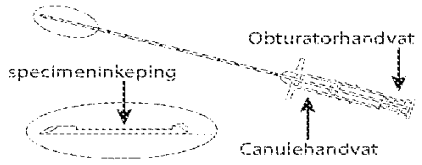
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TRU-CUT®

Dutch

Biopsienaalden voor zacht weefsel

GEBRUIKSINSTRUCTIES



GEBRUIKSINDICATIE:

De Tru-Cut®-biopsienaald voor zacht weefsel is een instrument dat via een canule wordt ingebracht in zacht weefsel zoals borst, longen, lymfeknopen en prostaat, enzovoort, voor diagnostische evaluatie.

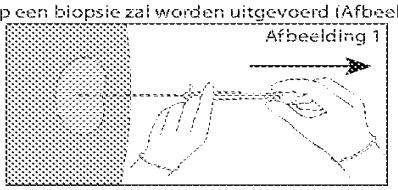
Waarschuwing: Deze naald is niet bedoeld om de huid te doorprikken. Te veel kracht of weerstand als de naald uitgetrokken wordt, kan leiden tot een gebogen specimeninkeping. Een gebogen specimeninkeping hindert de werking van de naald en kan leiden tot scheuren in het weefsel. Te veel laterale kracht op het obturatorhandvat van de naald uitoefenen kan de werking van het stopmechanisme hinderen en kan leiden tot een diepere insnijding in het weefsel dan gewenst is. Daardoor kan het weefsel of het orgaan worden beschadigd.

GEBRUIKSINSTRUCTIES:

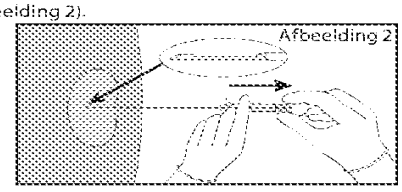
1. Maak de biopsielocatie klaar met behulp van een steriele techniek.
2. Verwijder de verpakking. Verwijder de beschermhuls.
3. Controleer op een juiste werking en plaatsing door de canule verschillende keren over de obturator te schuiven. Indien de onderdelen niet gemakkelijk bewegen, moet de eenheid worden weggegooid.

BIOPSIEPROCEDURE (BEHALVE VOOR BORSTBIOPSIE)

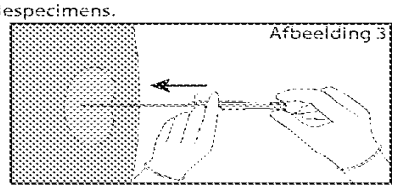
4. Trek de obturator terug zodat deze de specimeninkeping bedekt. Houd het canulehandvat vast en breng de naald in zodat de specimeninkeping zich in het weefsel bevindt waarop een biopsie zal worden uitgevoerd (Afbeelding 1).



5. Trek de canule terug zodat de specimeninkeping bloot komt te liggen. **Opmerking:** Beweeg de obturator niet (Afbeelding 2).

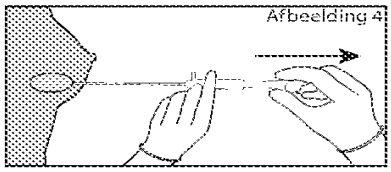


6. Om het weefsel te snijden, schuift u het canulehandvat snel vooruit (Afbeelding 3). Indien een tweede biopsie van hetzelfde weefsel vereist is, laat dan de canule op haar plaats, gericht naar de bedoelde biopsieplaats, en volg de instructies voor het afnemen van meerdere biopsiespecimens.

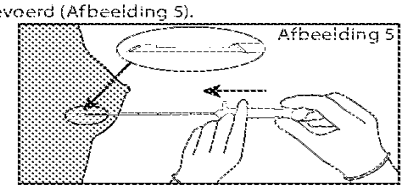


INSTRUCTIES VOOR BORSTBIOPSIE

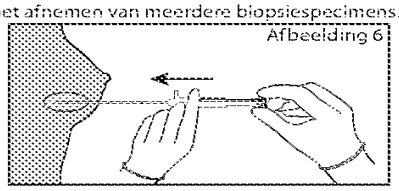
7. Trek de obturator terug zodat deze de specimeninkeping bedekt. Houd het canulehandvat vast en breng de naald in tot de rand van de biopsieplaats (Afbeelding 4).



8. Houd het canulehandvat stevig vast. Schuif de obturator zo ver als toegelaten vlug vooruit om de specimeninkeping in het weefsel te plaatsen waarop een biopsie zal worden uitgevoerd (Afbeelding 5).



9. Om het weefsel te snijden, schuift u het canulehandvat snel vooruit (Afbeelding 6). Indien een tweede biopsie van hetzelfde weefsel vereist is, laat dan de canule op haar plaats, gericht naar de bedoelde biopsieplaats, en volg de instructies voor het afnemen van meerdere biopsiespecimens.



VOOR MEERDERE BIOPSIESPECIMENS

- Houd het canulehandvat in een gefixeerde positie.
- Houd de obturatorschacht lichtjes omhoog zodat het stopmechanisme vrijkomt.
- Trek de obturator terug om deze van de canule te verwijderen.
- Verwijder het specimen uit de specimeninkeping.
- Om de obturator opnieuw in de canule te brengen, brengt u de obturatorschacht op één lijn met de open zijde van het canulehandvat en met de specimeninkeping naar omhoog gericht. Schuif de obturator naar voren tot de obturatorschacht in het handvat vastklikt.
- Volg één van de beschreven procedures voor het nemen van extra biopsiespecimens.

10. Trek de naald terug terwijl de canule nog steeds over de obturator geschoven is.
11. Schuif de obturator vooruit om het biopsiespecimen uit de specimeninkeping te verwijderen.

Waarschuwing:

- Niet geschikt voor gebruikt op bot.
- Niet gebruiken indien de verpakking beschadigd is.

LET OP: Uitsluitend voor eenmalig gebruik. Hergebruik kan ertoe leiden dat het product niet werkt en kan bijdragen aan kruisbesmetting.

Dit instrument mag alleen worden gebruikt door klinische artsen die de juiste training hebben ondergaan voor deze procedure, inclusief het voorbereiden van de patiënt, het bewaren van monsters en het gebruik van beeldgeleiding voor de percutane biopsie.

SYMBOOL	BETEKENIS
	Gebruiken vóór: JJJJ-MM-DD
LOT	Partijnummer
REF	Catalogusnummer
STERILE R	Gesteriliseerd met behulp van straling
	Niet gebruiken als de verpakking beschadigd is
	Voor eenmalig gebruik
℞ONLY	Let op: Onder de federale wetgeving van de Verenigde Staten mag dit instrument alleen worden verkocht op voorschrift van een arts.

Medisch apparaat.

Steriel pakket.

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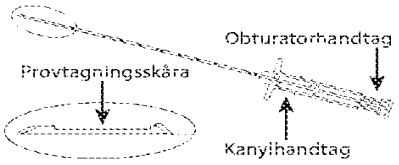
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TRU-CUT®

Swedish

Biopsinålar för mjukdelar

BRUKSANVISNING



INDIKATIONER FÖR ANVÄNDNING:
Tru-Cut® biopsinål för mjukvävnad är en enhet som inför en kanyl i mjukvävnad såsom bröst, lungor, lymfkörtlar och prostata etc. för diagnostisk utvärdering.

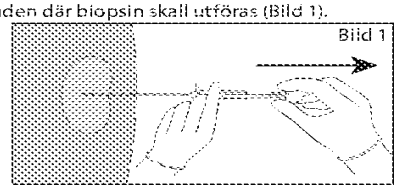
VARNING:
Denna nål är ej utformad för att punktera huden. Överdriven kraft eller motstånd när nålen dras ut kan medföra att provtagningsskåran böjs. En böjd provtagningsskåra hindrar nålens funktion och kan leda till att vävnaden skadas. Överdriven kraft anbringad mot sidan av nålens obturatorhandtag kan skada stoppmekanismens funktion, vilket kan resultera i en djupare vävnadspenetration än vad som önskas, med en potentiell risk för vävnads- eller organskada.

BRUKSANVISNING:

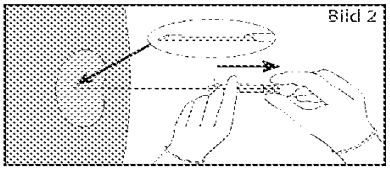
1. Använd steril teknik, förbered området för biopsin.
2. Avlägsna förpackningen. Avlägsna skyddshylsan.
3. Glid kanylen över obturator flera gånger för att säkerställa dig om att de fungerar ordentligt och är inriktade på korrekt sätt. Om delarna inte rör sig lätt, skall produkten kasseras.

BIOPSIPROCEDUR (EXKLUSIVE BRÖSTBIOPSI)

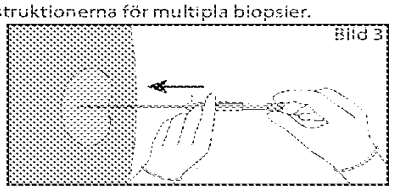
4. För tillbaka obturatorn för att skydda provtagningsskåran. Håll i kanylhandtaget och för in nålen och kanylen tillsammans så att provtagningsskåran befinner sig i vävnaden där biopsin skall utföras (Bild 1).



5. För tillbaka kanylen så att preparatfåran exponeras. **Obs!:** Rör ej obturatorn (Bild 2).

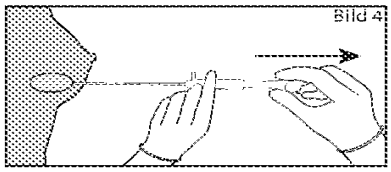


6. För provtagning, för snabbt in kanylhandtaget (Bild 3). Om ytterligare en biopsi på samma vävnad erfordras, lämnar du kanylen så att den är placerad vid området för biopsin och följ instruktionerna för multipla biopsier.

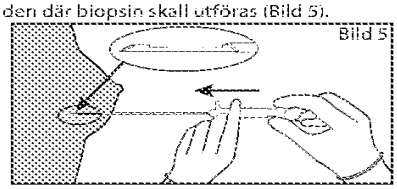


INSTRUKTION FÖR BRÖSTBIOPSI

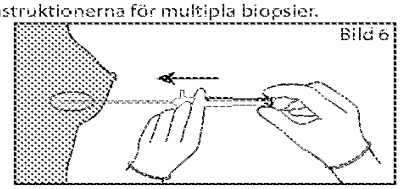
7. För tillbaka obturatorn för att skydda provtagningsskåran. Håll i kanylhandtaget och för in nålen och kanylen tillsammans till kanten för biopsiområdet (Bild 4).



8. Håll kanylhandtaget stadigt. För snabbt in obturatorn så långt som tillåts för att provtagningsskåran ska befinna sig i vävnaden där biopsin skall utföras (Bild 5).



9. För provtagning, för snabbt in kanylhandtaget (Bild 6). Om ytterligare en biopsi på samma vävnad erfordras, lämna kanylen så att den är placerad vid området för biopsin och följ instruktionerna för multipla biopsier.



FÖR MULTIPLA BIOPSIER

- Håll kanylhandtaget i ett fast läge.
- Lyft obturatorns skaft något så att stoppmekanismen frigörs.
- Dra tillbaka obturatorn för att avlägsna den från kanylen.
- Avlägsna preparatet från provtagningsskåran.
- För att föra obturatorn in i kanylen igen, rikta obturatorhandtaget så att den är i linje med kanylhandtagets öppna ände och provtagningsskåran är vänd uppåt. Skjut obturatorn inåt tills obturatorhandtaget låses fast vid kanylhandtaget.
- För ytterligare biopsier följer du en av provtagningsproceduerna ovan.

10. Dra tillbaka nålen över obturatorn, medan kanylen fortfarande befinner sig i utskjutet läge.
11. Skjut in obturatorn så att biopsipreparatet från preparatfåran kan avlägsnas.

VARNING:

- Ej avsedda för användning i ben.
- Får ej användas om förpackningen är skadad.

ENDAST FÖR ENGÅNGSBRUK. Återanvändning kan resultera i att produkten blir obrukbar eller bidra till korskontaminering.

Endast kliniker som har lämplig utbildning i detta förfarande, inklusive förberedelse av patienten, lagring av prov samt användning av bildvägledning för perkutan biopsi, bör använda denna anordning.

SYMBOL	BETECKNING
	Använd senast: YYYY-MM-ÅÅ
LOT	Partinummer
REF	Katalognummer
STERILE R	Steriliserad med bestrålning
	Använd inte om paketet är skadat
2	Engångsanvändning
℞ ONLY	Försiktighet: Enligt federal lag (i USA) får denna anordning endast säljas av eller på order av läkare.

Medicinsk anordning.
Steril förpackning.

CORBIN_CLINICAL-001138

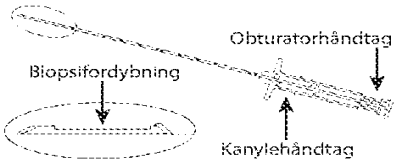
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TRU-CUT®

Danish

Bløddelsbiopsinåle

BRUGSANVISNING



INDIKATIONER:

Tru-Cut®-bløddelsbiopsinålen er en anordning, der indfører en kanyle i bløddele såsom bryst, lymfekirtel, lunge, prostata osv. med henblik på prøveudtagning.

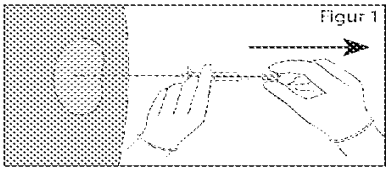
ADVARSEL: Denne nål er ikke designet til hudpunktur. For stor kraft eller modstand, når kanylen er trukket ud, kan resultere i bøjning af biopsifordybningen. En bøjet biopsifordybning vil kompromittere kanylens funktion og muligvis forårsage vævsskade. For stor sidekraft mod kanylens obturatorhåndtag kan kompromittere stopmekanismens funktion og kan resultere i dybere vævspenetration end ønsket med risiko for vævs- eller organskade.

BRUGSANVISNING:

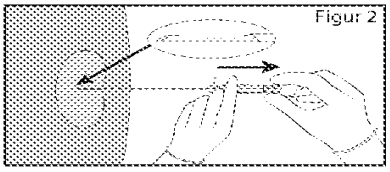
1. Klargør biopsistedet ved hjælp af en steril teknik.
2. Fjern emballagen. Fjern beskyttelsesrøret.
3. Test for korrekt funktion og justering ved at føre kanylen hen over obturatoren flere gange. Hvis delene ikke bevæger sig frit, skal anordningen kasseres.

BIOPSIINDGREB (UNDT. BRYSTBIOPSI)

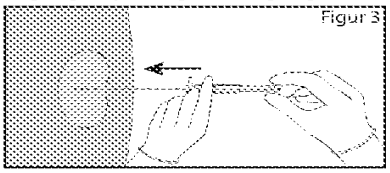
4. Træk obturatoren ud, så biopsifordybningen dækkes. Indsæt kanylen ved hjælp af kanylehåndtaget således, at biopsifordybningen er placeret inde i biopsivævet (Figur 1).



5. Træk kanylen ud, så biopsifordybningen blotlægges. **Bemærk:** Undlad at bevæge obturatoren (Figur 2).

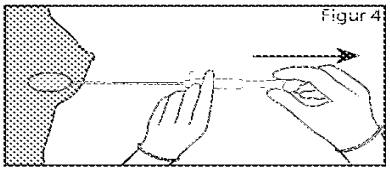


6. Vævet afskæres ved at føre kanylehåndtaget hurtigt fremad (Figur 3). Hvis det er nødvendigt at udtage en yderligere biopsi af det samme væv, skal man efterlade kanylen i den samme position og følge vejledningen i udtagning af flere biopsier.

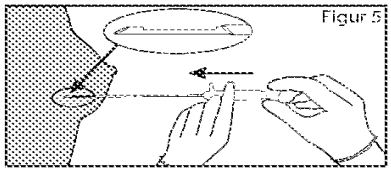


VEJLEDNING I BRYSTBIOPSI

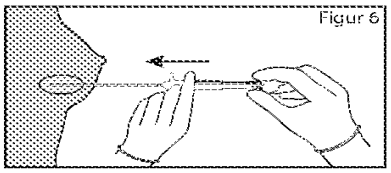
7. Træk obturatoren ud, så biopsifordybningen dækkes. Indsæt kanylen til kanten af biopsistedet ved hjælp af kanylehåndtaget (Figur 4).



8. Hold kanylehåndtaget på plads. Før obturatoren hurtigt fremad så langt som muligt for at positionere biopsifordybningen i biopsivævet (Figur 5).



9. Vævet afskæres ved at føre kanylehåndtaget hurtigt fremad (Figur 6). Hvis det er nødvendigt at udtage en yderligere biopsi af det samme væv, skal man efterlade kanylen i den samme position og følge vejledningen i udtagning af flere biopsier.



UDTAGNING AF FLERE BIOPSIER

- Hold kanylehåndtaget i fikseret position.
- Løft obturatorskaftet forsigtigt opad for at frigøre stopmekanismen.
- Træk obturatoren tilbage for at fjerne den fra kanylen.
- Fjern prøven fra biopsifordybningen.
- Obturatoren indsættes i kanylen igen ved at justere obturatorskaftet efter den åbne side af kanylehåndtaget og med biopsifordybningen opad. Skyd obturatoren fremad, indtil obturatorskaftet låses fast i håndtaget.
- Følg en af ovennævnte prøveudtagningsprocedurer for at udtage yderligere biopsier.

10. Træk nålen ud med kanylen stadig fremført over obturatoren.
11. Før obturatoren fremad for at fjerne biopsien fra biopsifordybningen.

ADVARSEL:

- Ikke beregnet til brug i knogler.
- Må ikke anvendes, hvis emballagen er beskadiget.

FORSIGTIG: Kun til engangsbrug. Genbrug kan resultere i et ikke-funktionsdygtigt produkt eller medvirke til krydskontaminering.

Kun klinikere, der er korrekt uddannet i dette indgreb, herunder klargøring af patienten, opbevaring af prøver og anvendelse af billeddiagnostik til perkutan biopsi, bør anvende denne anordning.

SYMBOL	BETYDNING
	Udløbsdato: ÅÅÅÅ-MM-DD
LOT	Partinummer
REF	Katalognummer
STERILE R	Steriliseret med bestråling
	Må IKKE anvendes, hvis emballagen er beskadiget
	Engangsbrug
℞ONLY	Forsigtig: Ifølge amerikansk (USA) lovgivning må denne anordning kun sælges eller ordineres af en læge.

Medicinsk udstyr.

Steril pakke.

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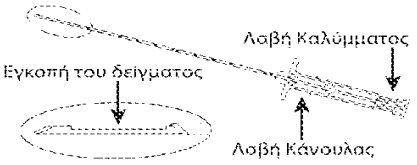
Advance Medical Designs, Inc. - EX1020
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TRU-CUT®

Greek

Βελόνες Βιοψίας Μαλακού Ιστού

ΟΔΗΓΙΕΣ ΧΡΗΣΗΣ



ΕΝΔΕΙΞΕΙΣ ΧΡΗΣΗΣ:

Η Βελόνα Βιοψίας Μαλακού Ιστού Tru-Cut® είναι μια διάταξη που εισάγει μια κάνουλα σε μαλακό ιστό, όπως οι μαστοί, οι πνεύμονες, οι λεμφαδένες, ο προστάτης κ.λπ, για διαγνωστική αξιολόγηση.

ΠΡΟΣΟΧΗ:

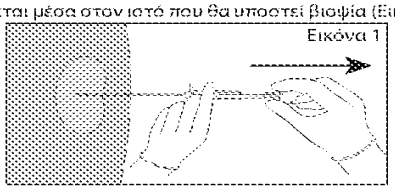
Αυτή η βελόνα δεν έχει σχεδιαστεί για διάτρηση του δέρματος. Υπερβολική δύναμη ή αντίσταση όταν η βελόνα είναι εκτεταμένη μπορεί να προκαλέσει κάμψη της εγκοπής του δείγματος. Αυτό μπορεί να επηρεάσει την λειτουργία της βελόνας και ίσως να σχίσει τον ιστό. Η υπερβολική πλευρική δύναμη που εφαρμόζεται στη λαβή του καλύμματος της βελόνας μπορεί να επηρεάσει τη λειτουργία του μηχανισμού διακοπής και μπορεί να οδηγήσει σε βαθύτερη είσοδο στον ιστό από ότι είναι επιθυμητό με πιθανή βλάβη των ιστών ή των οργάνων.

ΟΔΗΓΙΕΣ ΧΡΗΣΗΣ:

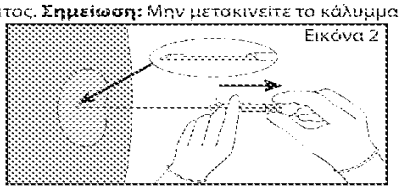
1. Προετοιμάστε το σημείο βιοψίας χρησιμοποιώντας άσηπτη τεχνική.
2. Αφαιρέστε τη συσκευασία. Αφαιρέστε το προστατευτικό περίβλημα.
3. Δοκιμάστε τη σωστή λειτουργία και την ευθυγράμμιση σύροντας την κάνουλα πάνω από το κάλυμμα αρκετές φορές. Αν τα μέρη δεν μετακινούνται εύκολα, τότε μη χρησιμοποιείτε τη συσκευή.

ΔΙΑΔΙΚΑΣΙΑ ΒΙΟΨΙΑΣ (ΕΚΤΟΣ ΒΙΟΨΙΑΣ ΜΑΣΤΟΥ)

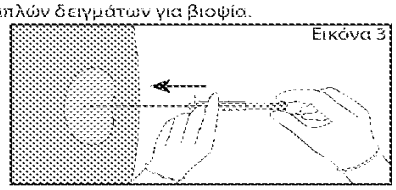
4. Τραβήξτε το κάλυμμα για να καλύψετε την εγκοπή του δείγματος. Κρατήστε τη λαβή της κάνουλας και τοποθετήστε το σύνολο της βελόνας μέσα έτσι ώστε η εγκοπή του δείγματος να βρίσκεται μέσα στον ιστό που θα υποστεί βιοψία (Εικόνα 1).



5. Τραβήξτε την κάνουλα έτσι ώστε να εμφανιστεί η εγκοπή του δείγματος. **Σημείωση:** Μην μετακινείτε το κάλυμμα (Εικόνα 2).

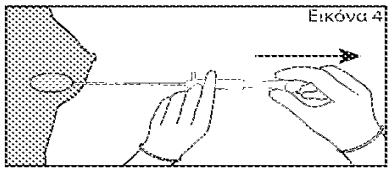


6. Για να κόψετε τον ιστό, προωθήστε γρήγορα την λαβή της κάνουλας (Εικόνα 3). Αν απαιτείται και άλλη βιοψία του ίδιου ιστού, αφήστε την κάνουλα τοποθετημένη στο συγκεκριμένο σημείο βιοψίας και ακολουθείστε τις οδηγίες για τη λήψη πολλαπλών δειγμάτων για βιοψία.

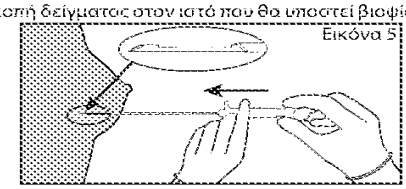


ΟΔΗΓΙΕΣ ΓΙΑ ΒΙΟΨΙΑ ΜΑΣΤΟΥ

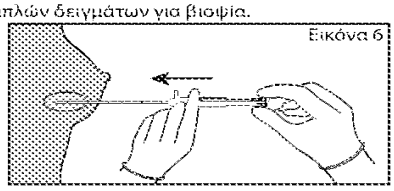
7. Τραβήξτε το κάλυμμα για να καλύψετε την εγκοπή του δείγματος. Κρατήστε τη λαβή της κάνουλας και τοποθετήστε το σύνολο της βελόνας στην άκρη του σημείου βιοψίας (Εικόνα 4).



8. Κρατήστε την λαβή της κάνουλας σταθερά. Γρήγορα μετακινήστε το κάλυμμα όσο επιτρέπεται ώστε να τοποθετηθεί η εγκοπή δείγματος στον ιστό που θα υποστεί βιοψία (Εικόνα 5).



9. Για να κόψετε τον ιστό, προωθήστε γρήγορα την λαβή της κάνουλας (Εικόνα 6). Αν απαιτείται και άλλη βιοψία του ίδιου ιστού, αφήστε την κάνουλα τοποθετημένη στο συγκεκριμένο σημείο βιοψίας και ακολουθείστε τις οδηγίες για τη λήψη πολλαπλών δειγμάτων για βιοψία.



ΓΙΑ ΠΟΛΛΑΠΛΑ ΔΕΙΓΜΑΤΑ ΒΙΟΨΙΑΣ

- Κρατήστε την λαβή της κάνουλας σε σταθερή θέση.
- Σηκώστε ελαφρά τον άξονα του καλύμματος για να καθαρίσετε τον μηχανισμό διακοπής.
- Τραβήξτε το κάλυμμα πίσω για να το αφαιρέσετε από την κάνουλα.
- Απομακρύνετε το δείγμα από την εγκοπή δειγμάτων.
- Για να επανατοποθετήσετε το κάλυμμα μέσα στην κάνουλα, ευθυγραμμίστε τον άξονα του καλύμματος με την ανοιχτή πλευρά της λαβής της κάνουλας και με την εγκοπή δειγμάτων να δείχνει προς τα επάνω. Σύρατε το κάλυμμα μπροστά μέχρι ο άξονας του να ασφαλίσει στη λαβή.
- Ακολουθήστε μία από τις διαδικασίες που περιγράφονται για να κάνετε συμπληρωματικές βιοψίες.

10. Αφαιρέστε το σύνολο της βελόνας με την κάνουλα ακόμα πάνω στο κάλυμμα.
11. Τραβήξτε μπροστά το κάλυμμα για να αφαιρέσετε το δείγμα από την εγκοπή.

ΠΡΟΣΟΧΗ:

- Να μην χρησιμοποιείται σε οστά.
- Μην το χρησιμοποιείτε, αν η συσκευασία έχει φθαρεί.

ΠΡΟΣΟΧΗ: Μόνο για μία χρήση. Αν επαναχρησιμοποιηθεί, ενδέχεται να προκληθεί βλάβη του προϊόντος ή διασταυρούμενη επιμόλυνση.

Αυτή η συσκευή πρέπει να χρησιμοποιείται μόνο από κλινικούς ιατρούς που έχουν λάβει κατάλληλη εκπαίδευση για αυτή τη διαδικασία, η οποία περιλαμβάνει την προετοιμασία του ασθενούς, τη διατήρηση του δείγματος και τη χρήση απεικονιστικής καθοδήγησης κατά τη δισδερμική βιοψία.

ΣΥΜΒΟΛΟ	ΧΑΡΑΚΤΗΡΙΣΜΟΣ
	Χρήση έως: ΗΗ-ΜΜ-ΕΕΕΕ
LOT	Αριθμός παρτίδας
REF	Αριθμός καταλόγου
STERILE R	Αποστειρωμένο με ακτινοβολία
	Μην χρησιμοποιείτε το προϊόν εάν η συσκευασία είναι κατεστραμμένη
	Μίας χρήσεως
℞ ONLY	Προσοχή: Η ομοσπονδιακή νομοθεσία των Η.Π.Α. επιτρέπει την πώληση της συγκεκριμένης συσκευής μόνο από ιατρό ή κατόπιν εντολής ιατρού.

Ιατρική συσκευή

Στείρα συσκευασία.

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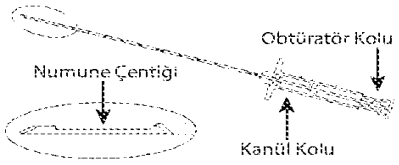
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TRU-CUT®

Turkish

Yumuşak Doku Biyopsi İğneleri

KULLANMA TALİMATLARI



KULLANIM ENDİKASYONLARI:

Tru-Cut® Yumuşak Doku Biyopsi İğnesi, tanısal değerlendirme amacıyla bir kanülün meme, akciğer, lenf düğümleri ve prostat gibi yumuşak dokuların içine sokulmasını sağlayan bir cihazdır.

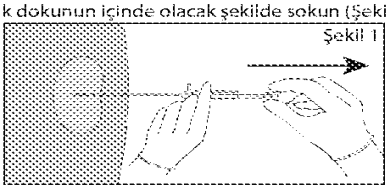
UYARI: Bu iğne deriyi delmek için tasarlanmamıştır. İğne ilerletildiğinde hissedilen aşırı kuvvet veya direnç, numune çentiğinin bükülmesine neden olabilir. Bükülmüş numune çentiği iğne işlevini engeller ve dokunun yırtılmasına neden olabilir. İğnenin obtüratör koluna aşırı yanal kuvvet uygulanması, durdurma mekanizmasının çalışmasını engelleyebilir ve dokunun istenilenden daha derin bir şekilde delinmesine ve neticesinde dokunun veya organın hasar görmesine neden olabilir.

KULLANMA TALİMATLARI:

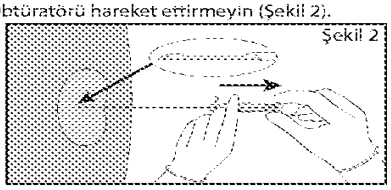
1. Steril teknik kullanarak biyopsi bölgesini hazırlayın.
2. Ambalajı çıkarın. Koruyucu kılıfı çıkarın.
3. Kanülü obtüratörün üzerinde birkaç kez kaydırarak düzgün çalıştığından ve hizalandığından emin olun. Parçalar kolayca hareket etmezse ürün atılmalıdır.

BİYOPSİ PROSEDÜRÜ (MEME BİYOPSİSİ HARİÇ)

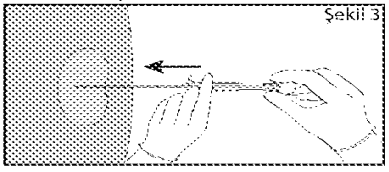
4. Obtüratörü numune çentiğini kapatacak şekilde çekin. Kanül kolunu tutun ve iğne mekanizmasını numune çentiği biyopsi alınacak dokunun içinde olacak şekilde sokun (Şekil 1).



5. Kanülü numune çentiği açığa çıkana kadar çekin.
Not: Obtüratörü hareket ettirmeyin (Şekil 2).

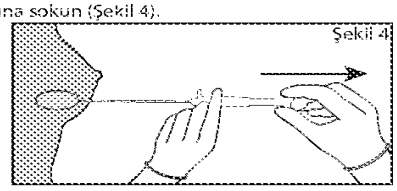


6. Dokuyu kesmek için kanül kolunu hızlıca ilerletin (Şekil 3). Aynı dokudan başka bir biyopsi alınması gerekiyorsa kanülü hedef biyopsi bölgesinde tutun ve birden fazla biyopsi örneği almaya ilişkin talimatları izleyin.

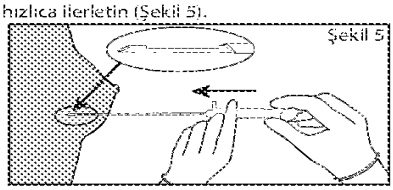


MEME BİYOPSİSİNE İLİŞKİN TALİMATLAR

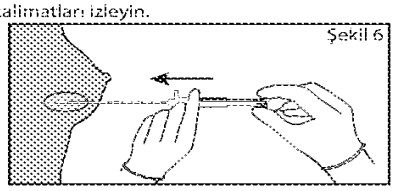
7. Obtüratörü numune çentiğini kapatacak şekilde çekin. Kanül kolunu tutun ve iğne mekanizmasını biyopsi bölgesinin kenarına sokun (Şekil 4).



8. Kanül kolunu sıkıca tutun. Numune çentiğini biyopsi alınacak dokuya yerleştirmek için obtüratörü mümkün olduğunca uzağa hızlıca ilerletin (Şekil 5).



9. Dokuyu kesmek için kanül kolunu hızlıca ilerletin (Şekil 6). Aynı dokudan başka bir biyopsi alınması gerekiyorsa kanülü hedef biyopsi bölgesinde tutun ve birden fazla biyopsi örneği almaya ilişkin talimatları izleyin.



BİRDEN FAZLA BİYOPSİ NUMUNESİ İÇİN

- Kanül kolunu sabit bir pozisyonda tutun.
- Durdurma mekanizmasını açmak için obrüratör milini yavaşça kaldırın.
- Obtüratörü geri çekerek kanülden çıkarın.
- Örneği numune çentiğinden çıkarın.
- Obtüratörü kanüle tekrar takmak için kanül kolunun açık tarafı ve numune çentiği yukarı bakarken obtüratör milini hizalayın. Obtüratör mili kola kilitlenene kadar obtüratörü ileri kaydırın.
- Başka biyopsi almak için açıklanan numune alma prosedürlerinden birini izleyin.

10. Kanülü obtüratörün üzerinden ilerletilmiş halde tutarak iğne mekanizmasını çekin.
11. Biyopsi örneğini numune çentiğinden çıkarmak için obtüratörü ilerletin.

UYARI:

- Kemikte kullanıma yönelik değildir.
- Ambalaj zarar görmüşse kullanmayın.

DİKKAT: Yalnızca tek kullanımlıktır. Tekrar kullanılması ürünün çalışmamasına veya çapraz kontaminasyona neden olabilir.

Bu ürün yalnızca hastanın hazırlanması, numunenin korunması ve perkütan biyopside görüntüleme rehberliğinden yararlanma dâhil olmak üzere bu prosedür konusunda doğru eğitimi almış klinisyenler tarafından kullanılmalıdır.

SEMBOL	TANIM
	Son Kullanma Tarihi: YYYY-AA-GG
LOT	Lot Numarası
REF	Katalog Numarası
STERILE R	İrradyasyon kullanılarak sterilize edilmiştir
	Ambalaj Hasar Görmüşse Kullanmayın
	Tek Kullanımlıktır
℞ONLY	Dikkat: Federal (ABD) yasalar uyarınca bu cihaz sadece hekim tarafından veya hekimin talimatı üzerine satılabilir.

Tıbbi Cihaz.

Steril Ambalaj.

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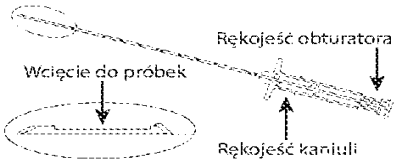
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TRU-CUT®

Polish

igły do biopsji tkanek miękkich

INSTRUKCJA UŻYTKOWANIA



WSKAZANIA DO STOSOWANIA:
Igła do biopsji tkanek miękkich Tru-Cut® to wyrób, który umożliwia wprowadzenie kaniuli do tkanek miękkich, takich jak piersi, płuca, węzły chłonne, prostata itp. w celu przeprowadzenia oceny diagnostycznej.

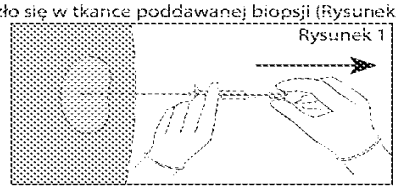
OSTRZEŻENIE: Ta igła nie jest przeznaczona do nakłuwania skóry. Nadmierna siła lub opór, kiedy igła jest rozłożona może powodować wygięcie wcięcia do próbek. Wygięte wcięcie do próbek będzie zakłócać funkcjonowanie igły i może spowodować rozdarcie tkanki. Zastosowanie nadmiernej siły bocznej na rękojeść obturatora igły może zakłócać funkcjonowanie mechanizmu zatrzymania i powodować głębszą penetrację tkanki niż jest to pożądane z możliwością uszkodzenia tkanek lub organów.

INSTRUKCJA UŻYTKOWANIA:

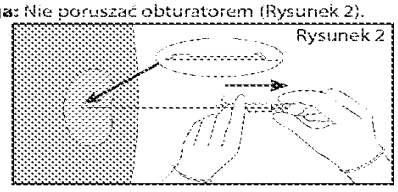
1. Przygotować miejsce wykonania biopsji, stosując sterylną technikę.
2. Zdjąć opakowanie. Zdjąć osłonę.
3. Sprawdzić pod względem prawidłowego funkcjonowania i wyrównania, kilkakrotnie wsuwając kaniulę na obturator. Jeśli części nie przesuwają się z łatwością, należy wyrzucić igłę.

PROCEDURA BIOPSJI (Z WYJĄTKIEM BIOPSJI PIERSI)

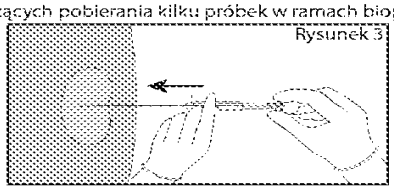
4. Wycofać obturator, aby zakryć wcięcie do próbek. Przytrzymać rękojeść kaniuli i włożyć zespół igły, aby wcięcie do próbek znalazło się w tkance poddawanej biopsji (Rysunek 1).



5. Wycofać kaniulę, aby odsłonić wcięcie do próbek.
Uwaga: Nie poruszać obturatorem (Rysunek 2).

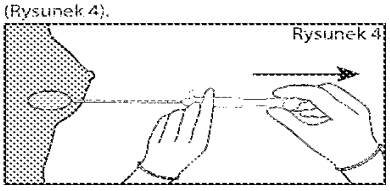


6. Aby przeciąć tkankę, szybko przesunąć rękojeść kaniuli w przód (Rysunek 3). Jeśli wymagane jest wykonanie jeszcze jednej biopsji tego samego rodzaju, pozostawić kaniulę w docelowym miejscu biopsji i postępować według instrukcji dotyczących pobierania kilku próbek w ramach biopsji.



INSTRUKCJE PRZEPROWADZENIA BIOPSJI PIERSI

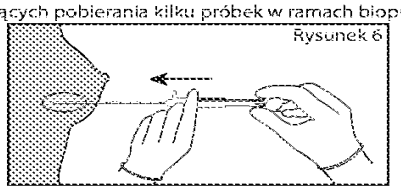
7. Wycofać obturator, aby zakryć wcięcie do próbek. Przytrzymać rękojeść kaniuli i umieścić zespół igły przy krawędzi miejsca biopsji (Rysunek 4).



8. Mocno przytrzymać rękojeść kaniuli. Szybko przesunąć obturator możliwie jak najdalej, aby ustawić wcięcie do próbek w tkance, z której ma zostać pobrana próbka (Rysunek 5).



9. Aby przeciąć tkankę, szybko przesunąć rękojeść kaniuli w przód (Rysunek 6). Jeśli wymagane jest wykonanie jeszcze jednej biopsji tego samego rodzaju, pozostawić kaniulę w docelowym miejscu biopsji i postępować według instrukcji dotyczących pobierania kilku próbek w ramach biopsji.



POBIERANIE KILKU PRÓBEK W RAMACH BIOPSJI

- Przytrzymać rękojeść kaniuli w stałej pozycji.
- Lekko unieść trzonek obturatora, aby oczyścić mechanizm zatrzymania.
- Odciągnąć obturator, aby wyjąć go z kaniuli.
- Wyjąć próbkę z wcięcia do próbek.
- Aby ponownie włożyć obturator do kaniuli, wyrównać trzonek z otwartą stroną rękojeści kaniuli, tak aby wcięcie do próbek było skierowane w górę. Wsunąć obturator w przód, dopóki trzonek obturatora nie zablokuje się w rękojeści.
- Postępować zgodnie z opisanymi procedurami w celu pobrania dodatkowych próbek.

10. Wycofać zespół igły, tak aby kaniula była nadal przesunięta na obturatorze.
11. Przesunąć obturator w przód, aby wyjąć pobraną próbkę z wcięcia do próbek.

OSTRZEŻENIE:

- Wyrób nie jest on przeznaczony do użycia wewnątrz kości.
- Nie używać w przypadku uszkodzenia opakowania.

PRZESTROGA: Wyłącznie do jednorazowego użytku. Ponowne użycie może spowodować nieprawidłowe działanie produktu lub zanieczyszczenie krzyżowe.

Wyrób mogą użytkować wyłącznie lekarze, którzy zostali odpowiednio przeszkoleni w zakresie tego zabiegu, w tym w zakresie przygotowania pacjenta, zachowania próbki i stosowania obrazowania do wykonania biopsji przezskórnej.

SYMBOL	PRZEZNACZENIE
	Użyć przed: RRRR-MM-DD
LOT	Numer partii
REF	Numer katalogowy
STERILE R	Sterylizowany przez naświetlanie
	Nie używać w przypadku uszkodzenia opakowania.
	Wyrób jednorazowego użytku
℞ONLY	Przestroga: Zgodnie z prawem federalnym Stanów Zjednoczonych niniejszy wyrób może być sprzedawany wyłącznie przez lekarza lub na zlecenie lekarza

Urządzenie medyczne.

Opakowanie jałowe.

CORBIN_CLINICAL-001142

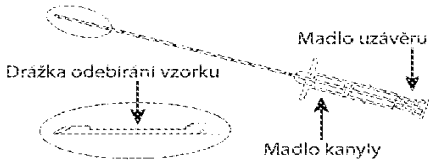
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TRU-CUT®

Czech

Bioptické jehly pro měkké tkáně

NÁVOD K POUŽITÍ



INDIKACE PRO POUŽITÍ:

Bioptická jehla pro měkké tkáně Tru-Cut® je zařízení, které zavádí kanylu do měkké tkáně jako jsou prsa, plíce, lymfatické uzliny, prostata apod. pro diagnostické zhodnocení.

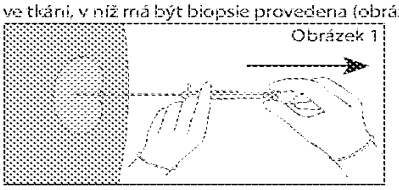
VAROVÁNÍ: Tato jehla není určena k propichování kůže. Přílišná síla nebo odpor v době, kdy je jehla vysunuta, může mít za následek ohnutí drážky odebírání vzorku. Ohnutá drážka odebírání vzorku brání řádné funkci jehly a může způsobit přetržení tkáně. Příliš vysoká boční síla působící proti ovládacímu prvku uzávěru může bránit řádné funkci dorazového mechanismu a může mít za následek hlubší vniknutí do tkáně, než je žádoucí, s nebezpečím poškození tkáně nebo orgánu.

NÁVOD K POUŽITÍ:

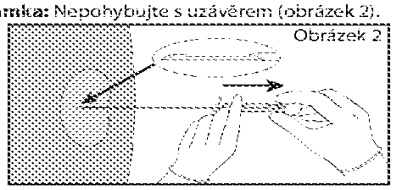
1. Sterilním postupem připravte místo biopsie.
2. Sejměte obal. Sejměte ochrannou fólii.
3. Vyzkoušejte správnou funkci a slícování několikerým posunutím kanyly přes uzávěr. Pokud se díly nepohybují lehce, je nutno nástroj vyhodit.

POSTUP BIOPSIE (KROMĚ BIOPSIE PRSOU)

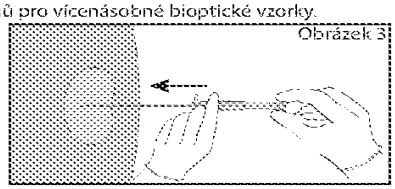
4. Zatáhněte uzávěr za účelem zakrytí drážky odběru vzorku. Držte madlo kanyly a zasuňte sestavu jehly tak, aby byla drážka odběru vzorku ve tkáni, v níž má být biopsie provedena (obrázek 1).



5. Zatáhněte kanylu za účelem odhalení drážky odběru vzorku. **Poznámka:** Nepohybujte s uzávěrem (obrázek 2).

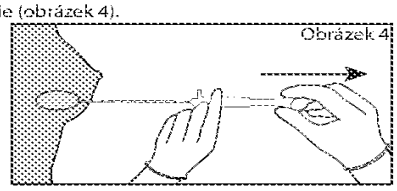


6. Uřízněte tkáň rychlým posunutím madla kanyly dopředu (obrázek 3). Pokud je nutná další biopsie stejné tkáně, nechte kanylu umístěnou na cílovém místě biopsie a postupujte dle pokynů pro vícenásobné bioptické vzorky.

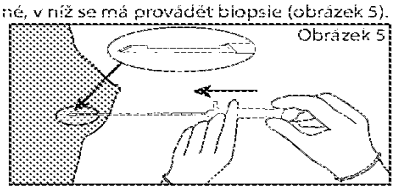


POKYNY PRO BIOPSII PRSOU

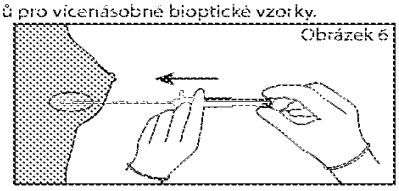
7. Zatáhněte uzávěr za účelem zakrytí drážky odběru vzorku. Držte madlo kanyly a zasuňte sestavu jehly na okraj místa biopsie (obrázek 4).



8. Pevně držte madlo kanyly. Rychle posuňte uzávěr dopředu tak dopředu, jak je to možné, pro nasazení drážky odběru vzorku do tkáně, v níž se má provádět biopsie (obrázek 5).



9. Uřízněte tkáň rychlým posunutím madla kanyly dopředu (obrázek 6). Pokud je nutná další biopsie stejné tkáně, nechte kanylu umístěnou na cílovém místě biopsie a postupujte dle pokynů pro vícenásobné bioptické vzorky.



U VÍCENÁSOBNÝCH BIOPTICKÝCH VZORKŮ

- Držte madlo kanyly v určené poloze.
- Lehce zvedněte dřík uzávěru, a uvolněte tak dorazový mechanismus.
- Vytažením uzávěru dozadu jej vyndejte z kanyly.
- Sejměte vzorek z drážky odběru vzorku.
- Pro opětovné zasunutí uzávěru do kanyly slícujte dřík uzávěru s otevřenou stranou madla kanyly, drážka odběru vzorku míří nahoru. Posuňte uzávěr dopředu, dokud se dřík uzávěru nezajistí v madle.
- Další biopsie provádějte jedním z postupů odběru vzorků.

10. Stáhněte sestavu jehly se stále vysunutou kanylou přes uzávěr.
11. Posuňte uzávěr dopředu a vyjměte bioptický vzorek z drážky odběru vzorků.

VAROVÁNÍ:

- Není určen k použití v kosti.
- Zařízení nepoužívejte, pokud došlo poškození jeho obalu.

UPOZORNĚNÍ: Určeno pouze k jednorázovému použití. Opakované použití může mít za následek nefunkční výrobek nebo křížovou kontaminaci.

Tento nástroj by měli používat pouze klinič tí odborníci, kteří jsou řádně vyškoleni v tomto postupu, včetně přípravy pacienta, uchovávání vzorků a používání zobrazovacích metod pro perkutánní biopsii.

SYMBOL	OZNAČENÍ
	Spotřebujte do: RRRR-MM-DD
LOT	Číslo šarže
REF	Katalogové číslo
STERILE R	Sterilizováno zářením
	Nepoužívejte, pokud došlo k poškození obalu
	Jedno použití
℞ONLY	Upozornění: Dle federálních zákonů USA si tento prostředek může koupit nebo objednat výhradně lékař

Medicinské zařízení.

Sterilní balení.

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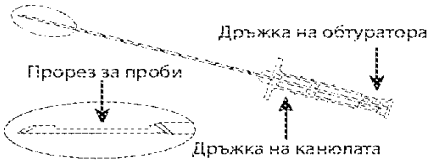
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TRU-CUT®

Bulgarian

Игли за биопсия на меки тъкани

ИНСТРУКЦИИ ЗА УПОТРЕБА



ПОКАЗАНИЯ ЗА УПОТРЕБА:
Иглата за биопсия на меки тъкани Tru-Cut® представлява устройство, което въвежда канюла в мека тъкан като гърди, бели дробове, лимфни възли, простата и др. за диагностична оценка.

ПРЕДУПРЕЖДЕНИЕ: Тази игла не е предназначена да пробива кожата. Прекомерната сила или съпротивление при вкарване на иглата може да доведе до огъване на прореза за проби. Огъването на прореза за проби ще попречи на функцията на иглата и може да доведе до разкъсване на тъканта. Прилагането на прекомерна латерална сила срещу дръжката на обтуратора на иглата може да попречи на функцията на стопиращия механизъм и да доведе до по-дълбоко от желаното пробиване на тъканта, както и потенциално до увреждане на тъканта или органа.

ИНСТРУКЦИИ ЗА УПОТРЕБА:

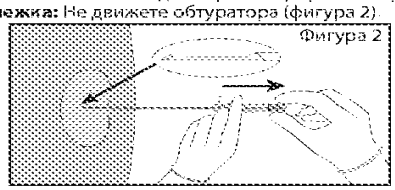
1. Подгответе мястото за биопсия, като използвате стерилна техника.
2. Махнете опаковката. Махнете защитната обвивка.
3. Изпробвайте правилната функция и подравняването, като плъзнете канюлата над обтуратора няколко пъти. Ако частите не се местят лесно, трябва да изхвърлите изделието.

ПРОЦЕДУРА ЗА БИОПСИЯ (С ИЗКЛЮЧЕНИЕ НА БИОПСИЯ НА ГЪРДИТЕ)

4. Изтеглете обтуратора, за да покрие прореза за проби. Хванете дръжката на канюлата и вкарайте иглата, така че прорезът за проби да се намира в тъканта за биопсия (фигура 1).



5. Изтеглете канюлата, за да откриете прореза за проби.
Забележка: Не движете обтуратора (фигура 2).

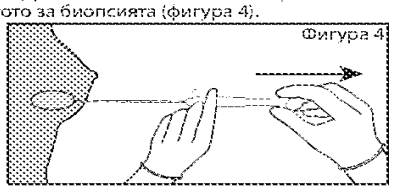


6. За да срежете тъканта, бързо придвижете напред дръжката на канюлата (фигура 3). Ако е нужна и друга биопсия на същата тъкан, оставете канюлата позиционирана спрямо целевото място за биопсия и следвайте инструкциите за няколко проби за биопсия.

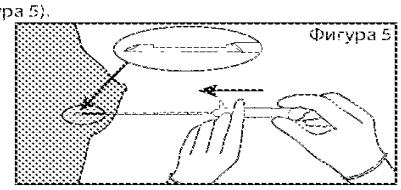


ИНСТРУКЦИИ ЗА БИОПСИЯ НА ГЪРДИТЕ

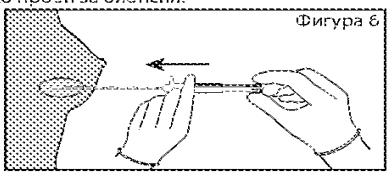
7. Изтеглете обтуратора, за да покрие прореза за проби. Хванете дръжката на канюлата и вкарайте иглата до края в мястото за биопсията (фигура 4).



8. Дръжте здраво дръжката на канюлата. Бързо придвижете напред обтуратора колкото е възможно най-много, за да позиционирате прореза за проби в тъканта за биопсия (фигура 5).



9. За да срежете тъканта, бързо придвижете напред дръжката на канюлата (фигура 6). Ако е нужна и друга биопсия на същата тъкан, оставете канюлата позиционирана спрямо целевото място за биопсия и следвайте инструкциите за няколко проби за биопсия.



ЗА НЯКОЛКО ПРОБИ ЗА БИОПСИЯ

- Задръжте дръжката на канюлата във фиксирана позиция.
- Повдигнете вала на обтуратора леко, за да почистите стопиращия механизъм.
- Издърпайте обтуратора назад, за да го извадите от канюлата.
- Извадете пробата от прореза за проби.
- За да вкарате отново обтуратора в канюлата, подравнете вала на обтуратора с отворената страна на дръжката на канюлата, като прорезът за проби трябва да гледа нагоре. Плъзнете обтуратора напред, докато валът му не се заключи в дръжката.
- Следвайте някоя от процедурите за вземане на проби, които са описани за вземане на допълнителни биопсии.

10. Изтеглете иглата, като канюлата все още е над обтуратора.
11. Придвижете обтуратора напред, за да извадите пробата за биопсия от прореза за проби.

ПРЕДУПРЕЖДЕНИЕ:

- Не е предназначена за употреба в костите.
- Не използвайте, ако опаковката е увредена.

ВНИМАНИЕ: Само за еднократна употреба. Повторната употреба може да доведе до нефункционален продукт или да допринесе за кръстосано заразяване.

Това изделие трябва да се използва само от клиницисти, които са надлежно обучени за тази процедура, включително и за подготвяне на пациента, запазване на пробите и използването на образни насоки за перкутанна биопсия.

СИМВОЛ	ОЗНАЧЕНИЕ
	Годно до: ГГГГ-ММ-ДД
LOT	Партиден номер
REF	Каталожен номер
STERILE R	Стерилизирано чрез облъчване
	Не използвайте, ако опаковката е увредена
	За еднократна употреба
℞ ONLY	Внимание: Федералният закон (САЩ) ограничава това устройство до продажба от или по предписание на лекар

Медицинско устройство.

Стерилна опаковка

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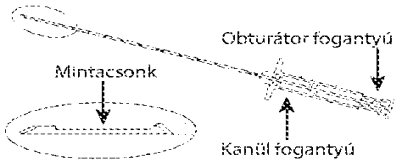
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TRU-CUT®

Hungarian

Lágyszöveti biopsziás tű

HASZNÁLATI UTASÍTÁS



ALKALMAZÁSI JAVALLATOK:

A Tru-Cut® puha szövet biopszia tű egy olyan eszköz, amely a diagnosztikai értékeléshez kanült vezet be a lágy szövetekbe, mint például az emlő, tüdő, nyirokcsomók és a dülmirigy.

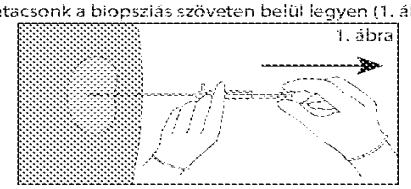
VIGYÁZAT: A tű nem alkalmas a bőr punkciójára. Ha a tűt meghosszabbították, a túlzott erő vagy ellenállás, hajlított mintacsonkhoz vezethet. A hajlított próbatest akadályozhatja a tű működését és szövetszakadást okozhat. Az obturátor fogantyúra gyakorolt túlzott oldalirányú erő megzavarhatja a leállító szerkezet működését, és a szövetek vagy a szervek károsodásának veszélyével járhat.

HASZNÁLATI UTASÍTÁS:

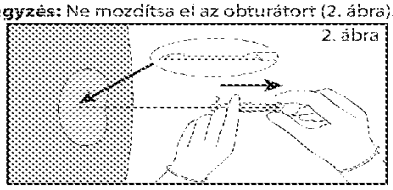
1. Steril technika alkalmazásával készítse elő biopsziás területet.
2. Távolítsa el a csomagolást. Távolítsa el a védőhüvelyt.
3. Ellenőrizze a helyes működést és az illeszkedést úgy, hogy a kanült többször végigcsúsztatja az obturátoron. Ha az összetevők mozgása akadályozott, az egységet hulladékra kell helyezni.

BIOPSZIÁS ELJÁRÁS (KIVÉVE AZ EMLŐBIOPSZIÁT)

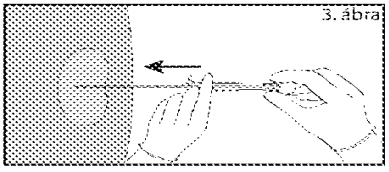
4. Húzza vissza az obturátort a mintacsonk lefedéséhez. Fogja meg a kanül fogantyúját, és tolja be a tűegységet úgy, hogy a mintacsonk a biopsziás szöveten belül legyen (1. ábra)



5. Húzza vissza a kanült, hogy felszabadítsa a mintacsonkot. **Megjegyzés:** Ne mozdítsa el az obturátort (2. ábra).

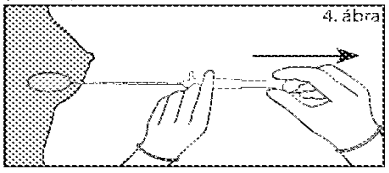


6. A szövet vágásához tolja gyorsan előre a kanül fogantyúját (3. ábra). Ha ugyanabból a szövetrészből kíván újabb biopsziát venni, hagyja a kanült a célbiopsziás helyen, és kövesse a többszörös mintavételre vonatkozó utasításokat.

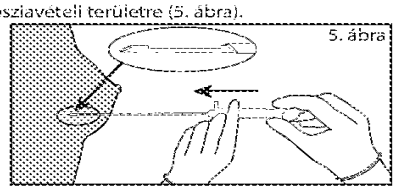


EMLŐBIOPSZIÁRA VONATKOZÓ UTASÍTÁSOK

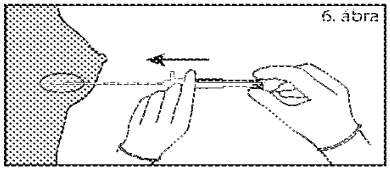
7. Húzza vissza az obturátort a mintacsonk lefedéséhez. A kanül fogantyúját megfogva tolja be a tűegységet a biopsziás terület széléig (4. ábra).



8. Tartsa stabilan a kanül fogantyúját. Gyorsan tolja előre az obturátort, amíg lehet, és helyezze a mintacsonkot a biopsziavételi területre (5. ábra).



9. A szövet vágásához tolja gyorsan előre a kanül fogantyúját (6. ábra). Ha ugyanabból a szövetrészből kíván újabb biopsziát venni, hagyja a kanült a célbiopsziás helyen, és kövesse a többszörös mintavételre vonatkozó utasításokat.



TÖBBSZÖRÖS BIOPSZIÁS MINTAVÉTEL

- Tartsa a kanül fogantyúját rögzített pozícióban.
- Enyhén emelje meg az obturátor tengelyét, hogy szabaddá tegye a zárószerkezetet.
- Húzza vissza az obturátort, hogy eltávolítsa a kanülből.
- Vegye ki a mintát a mintacsonkból.
- Az obturátor kanülbe történő visszahelyezéséhez illessze az obturátor tengelyét a kanül fogantyújának nyitott oldalához és a felfelé irányított mintacsonkhoz. Csúsztassa előre az obturátort, amíg az obturátor tengelye rögzül a fogantyúhoz.
- Kövesse a mintavételi eljárások egyikét, ha további biopsziát kíván végezni.

10. Húzza ki a tűegységet úgy, hogy a kanül az obturátor felett maradjon.
11. Tolja előre az obturátort, hogy eltávolítsa a biopsziás mintát a mintacsonkból.

VIGYÁZAT:

- Csontban történő használata nem javallt.
- Ne használja fel, ha a csomagolás sérült.

VIGYÁZAT! Csak egy betegen történő használatra. Az újrafelhasználás nem működő terméket eredményezhet, vagy hozzájárulhat a keresztszennyeződéshez.

Kizárólag olyan orvosok használják ezt az eszközt, akik megfelelő képzéssel rendelkeznek ehhez az eljáráshoz, beleértve a betegek előkészítését, a minta megőrzését és a képalkotásos útmutatás használatát a perkután biopsziához.

SZIMBÓLUM	JELENTÉS
	Felhasználható: ÉÉÉÉ.HH.NN.
LOT	Tételszám
REF	Katalógusszám
STERILE R	Besugárzással sterilizálva
	Ne használja, ha a csomagolás sérült.
	Egyszeri használat
℞ ONLY	Vigyázat! Az Amerikai Egyesült Államok szövetségi törvényeinek értelmében ez az eszköz kizárólag orvos által vagy orvosi rendelvényre értékesíthető.

Orvosi készülék.

Steril csomagolás.

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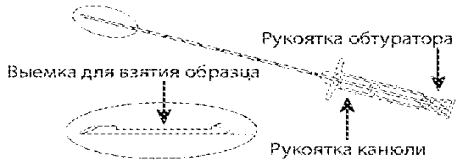
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TRU-CUT®

Russian

Иглы для биопсии мягких тканей

УКАЗАНИЯ ПО ПРИМЕНЕНИЮ



УКАЗАНИЯ ПО ПРИМЕНЕНИЮ:

Игла для биопсии мягких тканей Tru-Cut® представляет собой устройство для ввода канюли в мягкие ткани (такие, как молочная железа, легкие, лимфатические узлы, предстательная железа и пр.) для выполнения диагностической оценки.

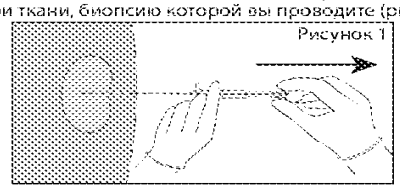
ПРЕДУПРЕЖДЕНИЕ: Данная игла не предназначена для прокалывания кожи. Чрезмерное усилие или сопротивление при выдвижении иглы может привести к изгибанию выемки для взятия образца. Изгибание выемки для взятия образца будет препятствовать нормальному функционированию иглы и может вызвать разрыв ткани. Приложение чрезмерного бокового усилия к рукоятке обтуратора иглы может препятствовать нормальной работе стопорного механизма и привести к более глубокому проникновению в ткань, чем это необходимо, с возможным повреждением тканей или органов.

УКАЗАНИЯ ПО ПРИМЕНЕНИЮ:

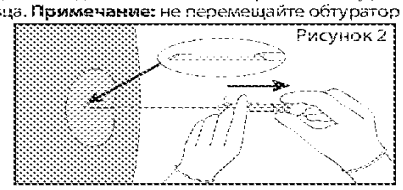
1. Подготовьте место для проведения биопсии, соблюдая стерильность.
2. Выньте изделие из упаковки. Снимите защитную оболочку.
3. Проверьте функционирование и регулировку, несколько раз переместив канюлю по обтуратору. Компоненты должны перемещаться легко, в противном случае изделие следует утилизировать.

ПРОЦЕДУРА БИОПСИИ (ЗА ИСКЛЮЧЕНИЕМ БИОПСИИ МОЛОЧНОЙ ЖЕЛЕЗЫ)

4. Отведите назад обтуратор, чтобы закрыть выемку для взятия образца. Взявшись за рукоятку канюли, введите иглу в сборе так, чтобы выемка для взятия образца оказалась внутри ткани, биопсию которой вы проводите (рисунок 1).



5. Отведите назад канюлю, чтобы открыть выемку для взятия образца. **Примечание:** не перемещайте обтуратор (рисунок 2).

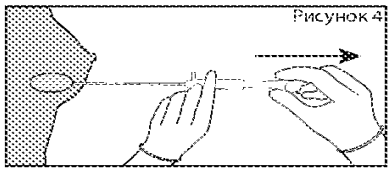


6. Чтобы вырезать ткань, быстро переместите вперед рукоятку канюли (рисунок 3). Если необходимо провести биопсию той же ткани еще раз, оставьте канюлю в месте проведения биопсии и следуйте указаниям по взятию нескольких биопсийных образцов.

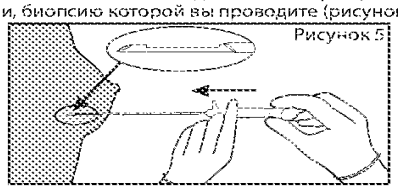


УКАЗАНИЯ ПО ПРОВЕДЕНИЮ БИОПСИИ МОЛОЧНОЙ ЖЕЛЕЗЫ

7. Отведите назад обтуратор, чтобы закрыть выемку для взятия образца. Взявшись за рукоятку канюли, введите иглу в сборе до границы места проведения биопсии (рисунок 4).



8. Крепко удерживайте рукоятку канюли. Быстро переместите вперед обтуратор на максимально разрешенное расстояние, чтобы выемка для взятия образца оказалась в ткани, биопсию которой вы проводите (рисунок 5).



9. Чтобы вырезать ткань, быстро переместите вперед рукоятку канюли (рисунок 6). Если необходимо провести биопсию той же ткани еще раз, оставьте канюлю в месте проведения биопсии и следуйте указаниям по взятию нескольких биопсийных образцов.



ВЗЯТИЕ НЕСКОЛЬКИХ БИОПСИЙНЫХ ОБРАЗЦОВ

- Удерживайте рукоятку канюли в неподвижном положении.
- Слегка поднимите ось обтуратора, чтобы освободить стопорный механизм.
- Вытяните обтуратор и извлеките его из канюли.
- Извлеките образец ткани из выемки для взятия образца.
- Чтобы вставить обтуратор обратно в канюлю, расположите ось обтуратора напротив открытого конца рукоятки канюли, так чтобы выемка для взятия образца была направлена вверх. Перемещайте обтуратор вперед, пока его ось не зафиксируется в рукоятке.
- Выполните одну из описанных процедур биопсии, чтобы взять дополнительные образцы ткани.

10. Извлеките иглу в сборе, при этом канюля должна быть по-прежнему перемещена по обтуратору вперед.
11. Переместите вперед обтуратор, чтобы извлечь биопсийный образец из выемки для взятия образца.

ПРЕДУПРЕЖДЕНИЕ:

- Не предназначены для биопсии костной ткани.
- Не используйте, если упаковка повреждена.

ВНИМАНИЕ! Предназначено только для одноразового использования. Повторное использование может привести к нарушению функционирования изделия или стать причиной перекрестного заражения.

Данное устройство должны использовать только медицинские работники, прошедшие соответствующую подготовку по выполнению указанной процедуры, включая подготовку пациента, сохранение образцов и применение визуального контроля для проведения чрескожной биопсии.

СИМВОЛ	ОБОЗНАЧЕНИЕ
	Срок годности: ГГГГ-ММ-ДД
LOT	Номер партии
REF	Номер по каталогу
STERILE R	Стерилизовано облучением
	Не использовать, если упаковка повреждена
	Для одноразового использования
℞ ONLY	Внимание! Федеральный закон США разрешает продажу данного устройства только врачам или по их назначению.

Изделие медицинского назначения.

Стерильная упаковка.

CORBIN_CLINICAL-001146

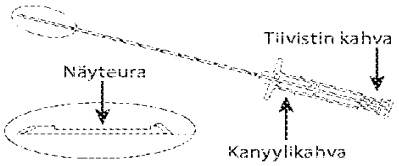
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TRU-CUT®

Finnish

Pehmytkudoksen biopsianeulat

KÄYTTÖOHJEET



KÄYTTÖAIHEET:

Tru-Cut®-pehmytkudosbiopsianeula on väline, joila kanyyli viedään pehmytkudokseen, kuten rintoihin, keuhkoihin, imusolmukkeisiin tai eturauhaseen, diagnostista arviointia varten.

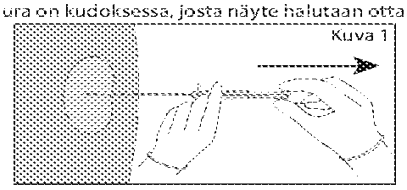
Varoitus: Tätä neulaa ei ole tarkoitettu ihon puhkaisemiseen. Voimankäyttö neulan ollessa ulkona saattaa aiheuttaa näyteuran taipumisen. Taipunut näyteura haittaa neulan toimintaa ja saattaa repiä kudosta. Voimakas neulan tiivistimen kahvan poikittaistyöntö saattaa haitata stopparimekanismin toimintaa ja neula saattaa tunkeutua syvemmälle kuin on toivottavaa mahdollisesti aiheuttaen kudos-tai elinvaurion.

KÄYTTÖOHJEET:

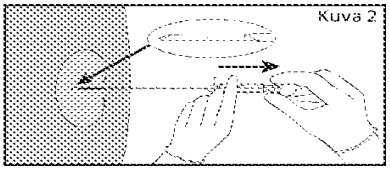
1. Valmistele biopsiakohta steriilisti.
2. Poista pakkaus. Poista suojakalvo.
3. Testaa toiminta ja suoralinjaisuus liu'uttamalla kanyyliä useita kertoja tiivistimen yli. Elleivät osat liiku vaivattomasti, neulaa ei tule käyttää.

BIOPSIAN SUORITTAMINEN (PAITSI RINTABIOPSIA)

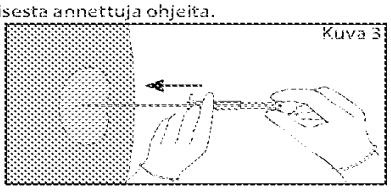
4. Vedä tiivistin näyteuran peitoksi. Pidä kiinni kanyylin kahvasta ja työnnä neulakokonaisuus sisään niin, että näyteura on kudoksessa, josta näyte halutaan ottaa (Kuva 1).



5. Vedä kanyyli ulos niin että näyteura paljastuu. **Huomaa:** Älä liikuta tiivistintä (Kuva 2).

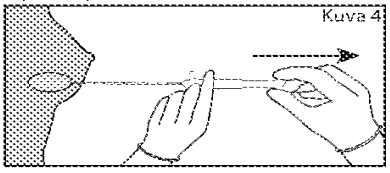


6. Leikkaa kudos työntämällä nopeasti kanyylin kahvasta (Kuva 3). Jos tarvitaan toinen näyte samasta kudoksesta, jätä kanyyli biopsiakohtaan ja seuraa useiden biopsianäytteiden ottamisesta annettuja ohjeita.

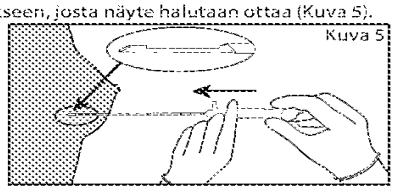


OHJEET RINTABIOPSIAAN

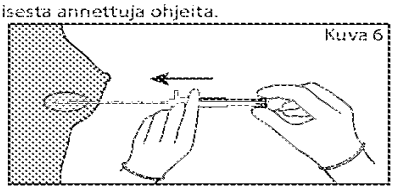
7. Vedä tiivistin näyteuran peitoksi. Pidä kiinni kanyylin kahvasta ja työnnä neulakokonaisuus biopsiakohdan reunaan (Kuva 4).



8. Ota kanyylin kahvasta tukeva ote. Työnnä nopeasti tiivistin niin pitkälle kuin se menee, jotta näyteura saadaan kudokseen, josta näyte halutaan ottaa (Kuva 5).



9. Leikkaa kudos työntämällä nopeasti kanyylin kahvasta (Kuva 6). Jos tarvitaan toinen näyte samasta kudoksesta, jätä kanyyli biopsiakohtaan ja seuraa useiden biopsianäytteiden ottamisesta annettuja ohjeita.



USEITA BIOPSIANÄYTTEITÄ OTETTAESSA

- Pidä kanyylin kahva kiinteässä asennossa.
- Nosta tiivistimen putkea hiukan stopparimekanismin avaamiseksi.
- Vedä tiivistimestä ja poista se kanyylistä.
- Poista näyte urasta.
- Työnnä tiivistin takaisin kanyyliin asettamalla tiivistimen putki linjaan kanyylin kahvan avoimen puolen kanssa näyteuran ollessa ylöspäin. Liu'uta tiivistintä eteenpäin kunnes tiivistimen putki lukittuu kahvaan.
- Noudata yllä mainittuja ohjeita lisänäytteiden ottamiseksi.

10. Vedä neulakokonaisuus ulos siten, että kanyyli on vielä tiivistimen päällä.
11. Työnnä tiivistintä niin, että näyte irtoaa näyteurasta. Ei saa käyttää, jos pakkaus on vaurioitunut.

Varoitus:

- Ei tarkoitettu käytettäväksi luuhun.
- Ei saa käyttää, jos pakkaus on vaurioitunut.

HUOMAUTUS: Vain kertakäyttöön. Uudelleen käyttäminen voi johtaa tuotteen toimimattomuuteen tai myötävaikuttaa ristikontaminaatioon.

Tätä laitetta tulisi käyttää ainoastaan kliinikot, jotka ovat saaneet asianmukaisen koulutuksen tämän menetelmän suorittamisessa, mukaanlukien potilaan valmistamisessa, näytteen säilönnässä ja kuvan ohjauksessa ihonläpäisevää biopsiaa varten.

MERKKI	SELITYS
	Viimeinen käyttöpäivä: VVVV-KK-PP
LOT	Eränumero
REF	Tuotenumero
STERILE R	Steriloitu säteilyttämällä
	Ei saa käyttää, jos pakkaus on vahingoittunut
	Kertakäyttöinen
℞ONLY	Huomio: Yhdysvaltain liittovaltion lain mukaan tämän laitteen saa myydä vain lääkäri tai lääkärin määräyksestä.

Lääkintälaite.

Steriili pakkaus.

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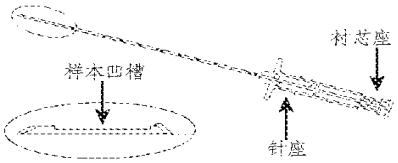
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TRU-CUT®

Chinese

软组织活检针

使用说明



使用说明：

Tru-Cut®软组织活检针是一种用于将针管插入胸部、肺部、淋巴结、前列腺等软组织以进行诊断性评价的器械。

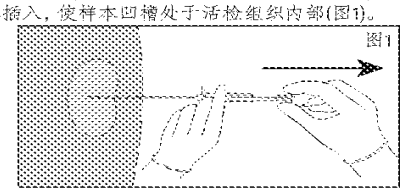
警告：本活检针的设计不适用于皮肤穿刺。当穿刺针处于伸出状态时，过度用力或者出现阻力能够引起样本凹槽的弯曲。样本凹槽弯曲会妨碍穿刺针的功能，并可能导致组织撕裂。对穿刺针的衬芯座过度侧向用力会妨碍制动机械装置的功能，并可能会使穿刺深度原于标记深度，有损伤组织或者器官的可能。

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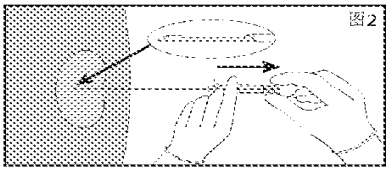
1. 使用无菌技术，对活检部位做好准备。
2. 拆开包装，移除保护鞘。
3. 检查功能是否正常，把针管套入衬芯直线滑动数次。如果有部件移动不畅，那么整套装置不应继续使用。

穿刺步骤（乳房穿刺除外）

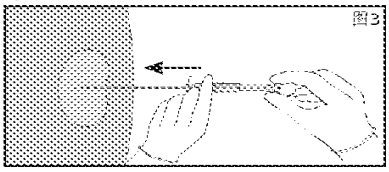
4. 回拉衬芯使样本凹槽处于遮盖状态。握住针座，把穿刺针组件整体插入，使样本凹槽处于活检组织内部(图1)。



5. 回拉针管使样本凹槽处于暴露状态。**注意：**不要移动衬芯(图2)。

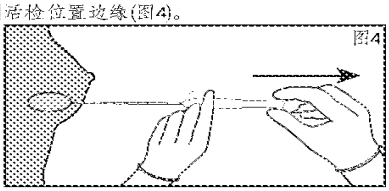


6. 快速推进针座以切割组织(图3)。如果需要对同一组织进行再次活检，则把针管放置于穿刺目标位置并按照多次穿刺取样的指导继续进行操作。

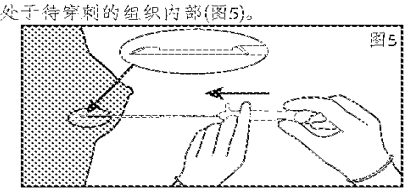


乳房穿刺的指导

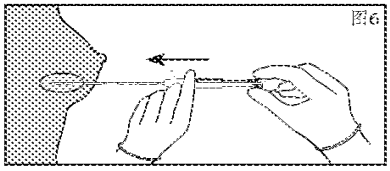
7. 回拉衬芯使样本凹槽处于遮盖状态。握住针座，把穿刺针组件插入到活检位置边缘(图4)。



8. 稳定地握住针座。快速推进衬芯，距离尽可能的长以便使样本凹槽处于待穿刺的组织内部(图5)。



9. 快速推进针座以切割组织(图6)。如果需要对同一组织进行再次活检，则把针管放置于穿刺目标位置并按照多次穿刺取样的指导继续进行操作。



多次穿刺取样的指导

- 握住针座使其处于一个固定位置。
- 轻轻抬起衬芯杆以清除制动机械装置。
- 回拉衬芯并把衬芯移出针管。
- 把样本从样本凹槽中移出。
- 使样本凹槽向上，把衬芯从针管开口处直线插入，以便使衬芯重新插入针管。把衬芯一直向前滑动推进，直到衬芯杆锁入手柄。
- 按照上述取样步骤中相应的程序继续操作以进行再次活检。

10. 把穿刺针组件撤出，撤出时要使针管相对于衬芯始终处于推进状态。
11. 推进衬芯，把活检样本从样本凹槽中移出。

警告：

- 不适用于骨活检。
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只有在本规程中经过适当培训的医生应当使用该器械，该规程包括病人准备、样本保存以及使用图像导引用于经皮活检。

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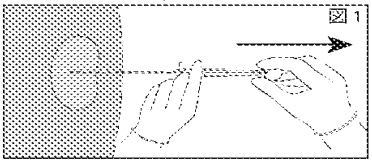
注意：この生検針は、皮膚を穿刺するようには作られておりません。針部を押し出す際に無理な力や抵抗を加えると、サンプル採取用ノッチの部分が曲がることがあります。サンプル採取用ノッチが曲がると標本の採取に支障を来し、切り取った組織が裂ける原因となることがあります。また、内針のつまみに側面から無理な力を加えると、自動停止機能が損なわれ、必要以上に深く組織を刺し過ぎてしまい組織もしくは器官を損傷する原因となることがあります。

使用方法：

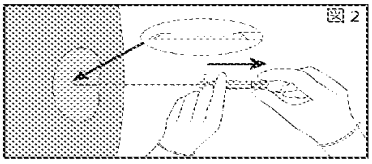
1. 無菌操作法をもって皮膚を消毒し、穿刺する部位を準備します。
2. 包装から生検針を取り出し、保護キャップをはずします。
3. 使用前に内針がなめらかに動くことを確かめます。もしなめらかに動かない場合はその製品を廃棄してください。

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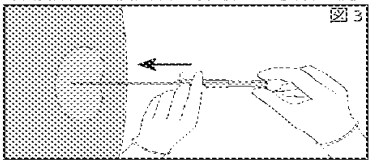
4. 内針を外管部内に完全に引き込み、サンプル採取用ノッチを外管部内に収めます。外管部のつまみを持って針を穿刺部位にあて、生検しようとする組織の中にサンプル採取用ノッチが入るように穿刺します（図 1）。



5. 外管部のつまみを手前に引いて、サンプル採取用ノッチを組織内に露出させます。**留意点：**内針を動かさないようにして下さい（図 2）。

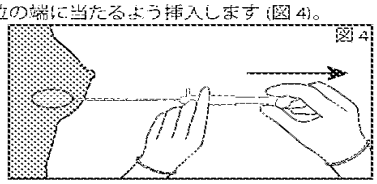


6. サンプル採取用ノッチ内に入った組織を切り取るために、外管部のつまみを素早く前方に押します（図 3）。同一の組織をもう一度採取する場合は、所定の生検部位に外管部をそのまま当て、複数の生検試料を採取する手順に従って下さい。

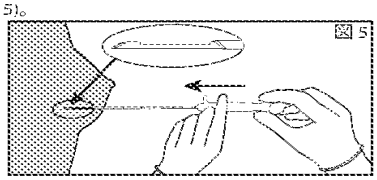


乳房生検法：

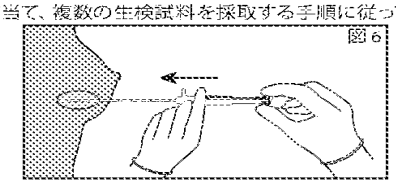
7. 内針を外管部内に完全に引き込み、サンプル採取用ノッチを外管部内に収めます。外管部のつまみを持ち、針が所定の穿刺部位の端に当たるよう挿入します（図 4）。



8. 外管部のつまみをしっかりと握り、サンプル採取用ノッチが所定の穿刺部位内に入るまで内針を素早く前方に押します（図 5）。



9. サンプル採取用ノッチ内に入った組織を切り取るために、外管部のつまみを素早く前方に押します（図 6）。同一の組織をもう一度採取する場合は、所定の生検部位に外管部をそのまま当て、複数の生検試料を採取する手順に従って下さい。



複数の生検試料を採取する場合：

- 外管部のつまみを一定の位置に保持します。
- 内針の柄を少し上方に持ち上げると、ストッパーがはずれて内針を引き抜くことが出来ます。
- 内針を手前に引き、外管部から内針を取りはずします。
- サンプル採取用ノッチから標本を取り出します。
- 内針の先端を外管部のつまみの入り口に合わせ、内針を外管部に再度挿入します。内針の柄がつまみに固定するまで内針を前方に進めます。
- 上述のいずれかの採取手順に従って、再度標本を採取します。

10. 内針は外管部に収納したまま針全体を抜去します。
11. 内針を前方に押し進め、標本をサンプル採取用ノッチから取り出します。

注意：

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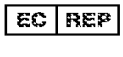


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Freehand Versus Guided Breast Biopsy: Comparison of Accuracy, Needle Motion, and Biopsy Time in a Tissue Model

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Anat Kornecki[3]
Allison Shaikh[3]
David Del Rey Fernandez[1]
Donald H. Taves[3]
Aaron Fenster[1–3]

OBJECTIVE. Freehand ultrasound-guided breast biopsy may present difficulties in needle visualization within the scanning plane of the ultrasound image. Scanning plane and needle misalignment, an unknown needle insertion site (relative to the ultrasound image), needle trajectory before insertion, and physician experience play roles in the difficulty of these biopsy procedures. The objective of our study was to compare the currently used freehand technique with the use of a needle guidance system that limits needle motion to within the ultrasound scanning plane for breast biopsy.

MATERIALS AND METHODS. We developed a needle guidance system for breast biopsy that is composed of an electronically tracked passive mechanical arm and braking mechanism. The system was attached to an ultrasound transducer, and biopsy needles were inserted through the guidance arm. Both experienced and inexperienced radiologists performed ultrasound-guided biopsy on simulated breast lesions with and without the guidance system. Success rates were scored on the basis of the presence of lesions in the core biopsy samples. The biopsy procedures were analyzed using procedure time and total needle tip travel distance before firing.

RESULTS. The biopsy success rates were greater using the guidance system ($p < 0.05$) than using the freehand technique. Experienced radiologists and inexperienced radiologists performed biopsy significantly faster using the needle guidance system ($p < 0.001$). Additionally, needle tip motion was significantly greater when using the freehand technique ($p < 0.001$) than using the guidance system.

CONCLUSION. Biopsy using the developed needle guidance system is feasible and its use decreases procedure time and decreases needle motion; thus, it has the potential to reduce patient morbidity. Moreover, less operator experience is required for a successful breast biopsy using the needle guidance system than using the freehand technique.

Keywords: breast biopsy, biopsy time, image guidance, needle motion, ultrasound biopsy

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Mammography screening subjects who present with suspicious breast lesions usually undergo imaging-guided biopsy using either stereotactic mammography or ultrasound guidance [1]. Ultrasound guidance is preferred because it provides real-time images, does not require ionizing radiation, and makes use of compact imaging instrumentation [2–7]. Radiologists performing biopsy on suspicious breast lesions by ultrasound use a freehand technique: A needle is guided to the target with one hand while the other hand positions the ultrasound transducer for adequate visualization [1]. Guidance under freehand conditions is challenging and may be time-consuming because of the necessity to align the scanning plane and needle axis [8]. The ultrasound scanning plane must remain coplanar with the needle axis for adequate visualization of the needle tip; thus, the experience of the physician dictates the success of the freehand ultrasound-guided biopsy procedure.

Guidance devices that attempt to overcome the challenges of freehand biopsy by restricting needle motion to varying degrees are available. Fixed-angle insertion is achieved with a needle guide: a plastic clip-on attachment (Ultra-Pro 3, CIVCO Medical Solutions) that permits needle insertion at a static angle relative to the ultrasound transducer scanning surface. With the attachment in place, the needle is limited to angled insertion toward targets located in the center of the ultrasound image, which prevents access to shallow and deep lesions. Han et al. [9] developed a rotary insertion wheel that attaches

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to the ultrasound transducer and permits angled and parallel insertion to overcome the limitations of fixed-angle insertion. The difficulty with this approach is the inability to insert the needle either close to the lesion or consistently parallel or anterior to the patient's chest wall to avoid potential chest wall or transducer puncture.

Additional solutions have been developed that provide relatively unrestrained biopsy: tracking the magnetic field of the imaging and needle components or displaying a line on the patient's skin corresponding to the ultrasound scanning plane [10, 11]. These unrestrained solutions may be challenging to use because they do not limit the needle to motion within the ultrasound scanning plane, resulting in difficulty aligning the needle and scanning plane similar to the freehand technique.

We developed a mechanical needle guidance system that couples a 2D ultrasound transducer to a needle. The system allows needle insertion at an unrestricted trajectory but constrains the needle to within the ultrasound scanning plane. Additionally, the electronically tracked needle trajectory is displayed as an overlay on real-time ultrasound images before and during needle insertion procedures.

In this article, our objective is to report the results of our study comparing the success rate, procedure time, needle tip travel distance, and physician experience of biopsy procedures in a tissue model. We compared these variables for freehand biopsy and needle-guided biopsy.

With the development of the attached system and visualized pathway, we endeavor to improve biopsy guidance and reduce the time of ultrasound-guided procedures. Additionally, we propose that this device can aid physicians by reducing the amount of experience required to perform a successful biopsy procedure.

Materials and Methods

Guidance System Development

The technical design and fabrication of the needle guidance device that we developed have been described in detail elsewhere [12] and are only summarized here. The device is a passive articulated arm that is fixed to a bracket attached to an ultrasound transducer. This arm is composed of three joints: one at the attachment bracket, one between two linkages, and one at the needle coupling point (Fig. 1). Sensors for real-time computation of the arm's position electronically track the rotational motion at each joint and, hence, the needle trajectory relative to a real-time ultrasound image. The computed needle trajectory is displayed as an overlay on top of the acquired ultrasound image and is used for guidance before and during needle insertion (Fig. 2). The accuracy of the guidance system allows targeting lesions 1.5 mm in diameter identified with an ultrasound transducer (L12-5 transducer, ATL) and an ultrasound machine (HDI 3500, Philips Healthcare) [12]. The same transducer and ultrasound machine were used in the studies reported here.

Simulated Lesion Study

Chicken tissue was used as a model owing to its similarity in echotexture and consistency to human tissue [13–15]. We used embedded simulated lesions made from blue polyvinyl alcohol cryogel chicken tissue [16]. Our previous study described preparation of this chicken phantom and the biopsy procedure in detail [12], we summarize these steps in the following sections.

Preparation of Lesions and Chicken Tissue Phantom

Lesions measuring 2 mm in diameter are clinically detectable under ultrasound guidance; thus, blue cylindric simulated lesions with a diameter and height of 2.5 mm were prepared from polyvinyl alcohol cryogel [17] (Fig. 3). The simulated lesions were inserted into chicken tissue after one freeze–thaw cycle using a method similar to that of Smith et al. [13].

We stabilized the phantom by layering the lesion-filled fowl tissue and affixing it to a foam block using 18-gauge needles. With this construction, "lesions" were positioned between 20 and 40 mm from the top tissue surface. Additionally, trapped air was removed using ultrasound acoustic coupling gel between each layer and within each hole where lesions had been inserted, which resulted in clear images of most lesions (Fig. 4). Only lesions that could be visualized were biopsied because the purpose of

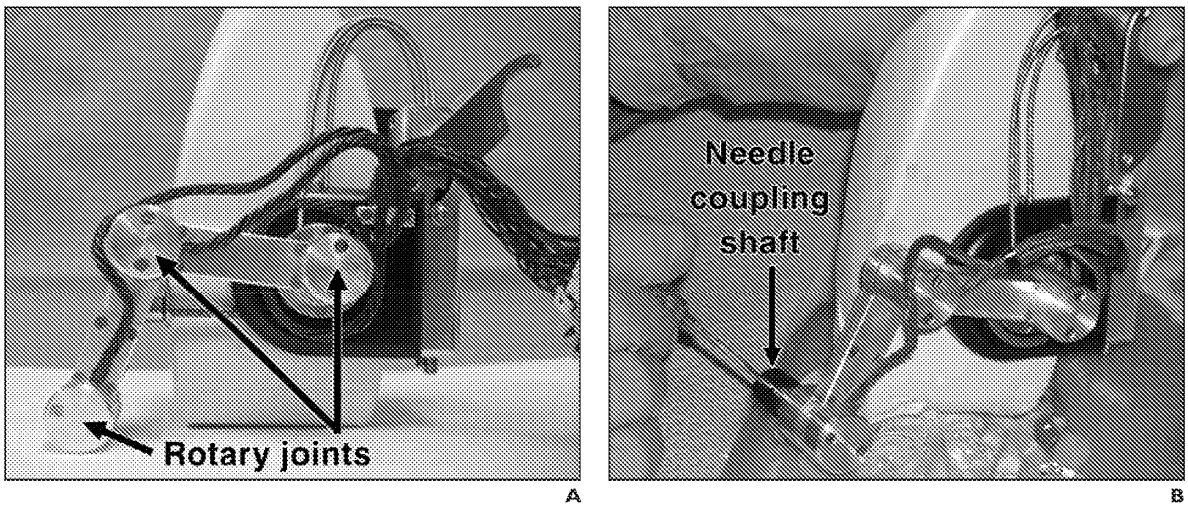


Fig. 1—Needle guidance system.
A, Photograph shows needle guidance system coupled to transducer (L12-5 transducer, ATL) with three rotational joints.
B, Photograph shows needle being inserted through coupling shaft. Needle motion is tracked electronically by passive mechanical arm.

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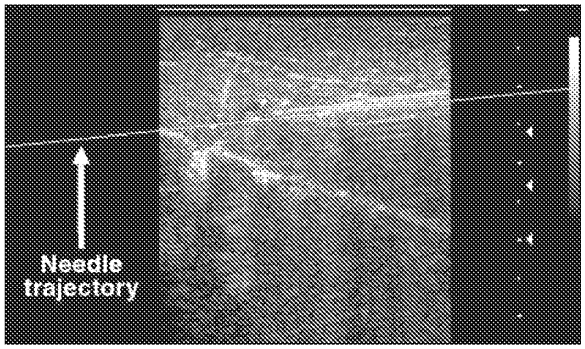


Fig. 2—Computed needle trajectory overlay is displayed on ultrasound image acquired in real time to enable guidance before and during interventional procedures.

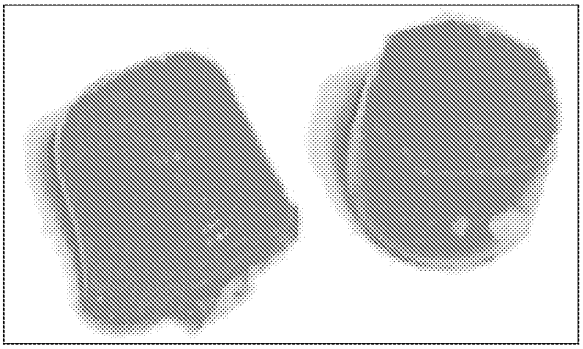


Fig. 3—Photograph shows blue polyvinyl alcohol cryogel lesions that were constructed using one freeze–thaw cycle. These "lesions" appear as hypoechoic masses when inserted into chicken test phantoms.

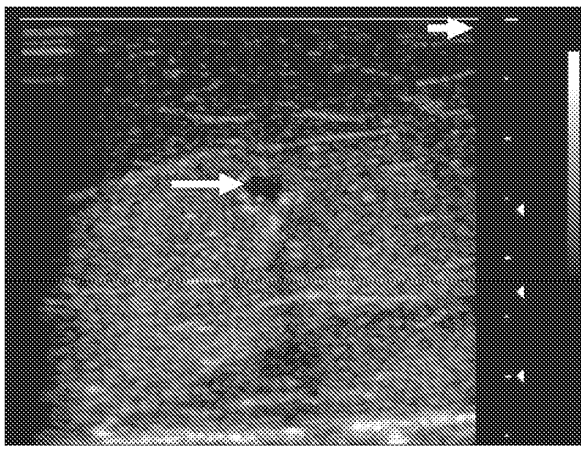


Fig. 4—Ultrasound image of polyvinyl alcohol cryogel–simulated lesion in chicken phantom. Hypoechoic characteristics of simulated lesion, indicated by long arrow, resemble those of clinical mass. Lesion distance was calculated from same reference pixel indicated by short arrow.

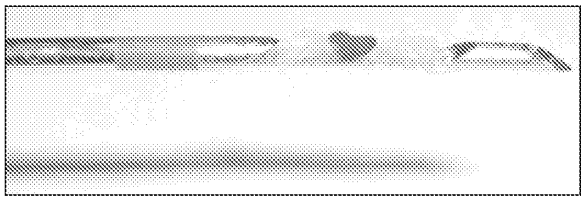


Fig. 5—Photograph shows core sample after biopsy. Blue polyvinyl alcohol cryogel–simulated lesion, situated between two pieces of phantom tissue, indicates successful biopsy.

this study was to evaluate procedure time and needle tip travel distance, not to identify lesions.

Three radiology residents without previous biopsy experience and two expert radiologists who routinely perform breast biopsies used the ultrasound transducer to scan the layered chicken breast phantom in B mode. Participants were alternately assigned to biopsy the first set of lesions with either a freehand technique or the needle guidance system, followed by biopsy using the other guidance technique not used for the first set of lesions.

Once a lesion of interest was identified, a preloaded 14-gauge biopsy needle inserted in a biopsy gun apparatus (Bard Magnum, Bard) was advanced by the physician. Video recording of the ultrasound images began once the needle tip made contact with the surface of the chicken tissue. A core biopsy was obtained by firing the biopsy gun once the needle tip was within firing distance of the target and video recording was terminated. A biopsy was deemed successful if any blue lesion material was present in the core sample (Fig. 5). This procedure was repeated 45 times per participant.

Using only procedure videos of successful biopsies and image frames of clear hypoechoic lesions, the average distance to the center of the lesion, measured from a reference point, was calculated. Procedure times for failures were not used because the reasons for failure were variable and could range from misfiring of the biopsy gun to improper alignment with the scanning plane. To maintain consistency of measurements across all depth settings, our selected reference point was the top right pixel of the image (Fig. 4). Pixel values were converted using a pixel-to-millimeter conversion factor specific to each ultrasound depth setting. Conversion factors were determined through measurement of a line of known pixel length using image calipers (HDI 3500). The approximate center of the lesion was identified and recorded, and the distance of the center of the lesion to the reference point was averaged in each of the procedure videos. These measurements were repeated for both guidance techniques for each participant.

Biopsy guidance was assessed on the basis of procedure time, which was defined as the time between the start of the procedure video when the biopsy needle touched the tissue phantom until the frame before the biopsy gun was fired. The order of biopsy attempts using each guidance technique was matched and grouped by biopsy success. Attempts were further sorted into pairs where lesions were within 2.5 mm of one another. A paired-samples Student's t test was used to compare the mean difference in success rates of each procedure because our data were found to be normal according to considerations provided by Brown et al. [18].

Needle Tip Travel Distance

The distance the needle tip moved was calculated using the same trials. The total distance

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TABLE 1: Biopsy Procedure Times for All Participants Using the Needle Guidance System and Using the Freehand Technique for Breast Biopsy

Participants	No. of Trials	Biopsy Procedure Time (s)		Wilcoxon's *Z* Statistic	*p*
		Mean	SD		
Experienced ($n = 2$)				−5.12	< 0.001
Needle guidance system	35	9.69	4.75		
Freehand technique	35	30.91	13.62		
Inexperienced ($n = 3$)				−5.61	< 0.001
Needle guidance system	42	6.00	5.25		
Freehand technique	42	22.86	18.33		

that a needle tip travels in a patient's tissue is indicative of the efficacy of the biopsy procedure. A needle that travels a large distance may indicate difficulties such as inability to maintain lesion visualization, scanning plane and needle misalignment, tissue inhomogeneity, or other visualization issues that are overcome by operator experience. We calculated the total needle tip travel distance caused by needle motion between the same time points and trials used in scoring the procedure time.

A frame-by-frame analysis of each procedure video, captured at a frame rate of 15 frames per second, was performed. If the needle tip was visible, its position was recorded; otherwise, the next video frame was examined. In the worst case, two frames would be missed, representing a temporal gap of 0.133 second: A time frame that does not alter the significance of our results. The distance from each previous point to the newly recorded point was summed until the last frame before biopsy gun firing. The final distance value was the total distance that the needle tip traveled from contact with the chicken phantom to the targeted lesion. This value was compared between guidance techniques (i.e., freehand vs needle guidance system) using the same biopsy attempts as in the procedure time analysis described.

Procedure times and needle tip travel distances were compared using the nonparametric Wilcoxon's signed rank test. Trials from each guidance technique were paired and grouped by participant experience. Mean values of the paired-sample difference were compared for each group's procedure times (i.e., experienced and inexperienced participants). Needle tip travel distances for experienced participants and inexperienced participants were calculated for comparison using the same pairing.

Results

Biopsy success rates were greater with the needle guidance system than with the freehand technique (mean, 95.9% vs 91.3%, respectively), and analysis by technique showed a statistically significant difference in the overall success rate in the two arms of our study ($p < 0.05$). The paired-samples 95% CI of the success rate difference was bounded below zero in the Student's *t* test, indicating significance.

Descriptive statistics for procedure time comparison analysis are shown in Table 1. Participants experienced with ultrasound biopsy had a mean procedure time of 30.91 ± 13.62 (SD) seconds when performing biopsy using a freehand technique and a mean procedure time of 9.69 ± 4.75 seconds when using the guidance system. Inexperienced participants had a mean procedure time of 22.86 ± 18.33 seconds and 6.00 ± 5.25 seconds for the freehand technique and needle guidance device, respectively. Rank ordered Wilcoxon's method results comparing procedure times indicated a significant difference in technique procedure time in both the experienced ($p < 0.001$) and inexperienced ($p < 0.001$) groups (Table 1). Comparisons of mean procedure times and procedure time

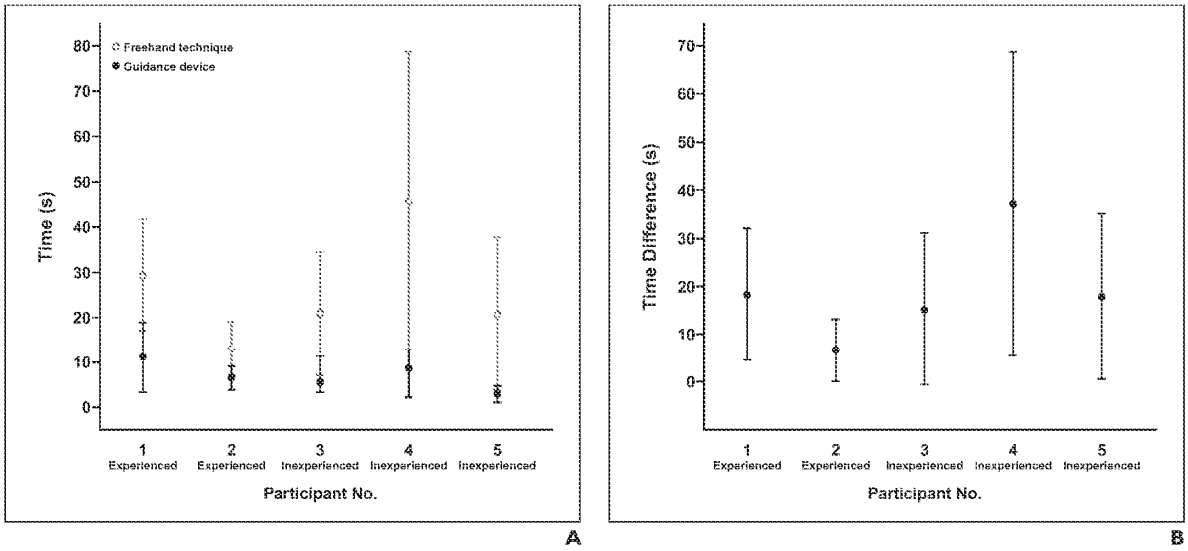


Fig. 6—Plots show results by individual participant.
A, Mean procedure times of all biopsy trials using different biopsy guidance techniques are shown for each participant. Error bars represent SDs.
B, Differences in mean procedure times were calculated by subtracting mean procedure time using needle guidance from mean procedure time using freehand technique.

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TABLE 2: Needle Tip Travel Distances for All Participants Using the Needle Guidance System and Using the Freehand Technique for Breast Biopsy

Participants	No. of Trials	Needle Tip Travel Distance (mm)		Wilcoxon's *Z* Statistic	*p*
		Mean	SD		
Experienced ($n = 2$)				−3.96	< 0.001
Needle guidance system	35	13.98	7.63		
Freehand technique	35	25.39	15.63		
Inexperienced ($n = 3$)				−5.25	< 0.001
Needle guidance system	42	11.81	7.85		
Freehand technique	42	33.24	23.73		

differences of both techniques for each participant are shown in Figure 6.

In the experienced group, mean tip travel distances of 25.39 ± 15.63 (SD) mm and 13.98 ± 7.63 mm were observed for the freehand technique and needle guidance device, respectively. Inexperienced participants performed biopsy with mean tip travel distances of 33.24 ± 23.73 mm and 11.81 ± 7.85 mm for the freehand technique and needle guidance system, respectively.

Additionally, descriptive statistics for needle tip travel distances are shown in Table 2. Needle tip travel distances for the freehand technique and needle guidance device were significantly different in both experienced ($p < 0.001$) and inexperienced ($p < 0.001$) groups (Table 2).

Tables 1 and 2 show consistently lower procedure times and needle tip travel distances with lower variance when using the needle guidance system regardless of operator experience.

Discussion

Our results indicate a longer biopsy time using the freehand technique compared with using our guidance system. This difference in procedure time may be attributed to several factors. When participants inserted the biopsy needle under freehand ultrasound guidance, they spent time aligning the ultrasound scanning plane and needle axis while attempting to maintain adequate visualization of the target lesion. Often, once either the needle or the target lesion was aligned with the ultrasound scanning plane, the other would disappear resulting in additional procedure time needed for realignment. Participants experienced in ultrasound breast biopsy had a longer procedure time than inexperienced participants because they were cautious to maintain visualization during biopsy, although the difficulty in scanning plane alignment remained. The needle guidance system eliminated the need to align the ultrasound scanning plane with the needle and displayed the needle trajectory before the insertion so that the participant could focus solely on guidance of the needle toward the intended target lesion. Thus, participants with and those without prior ultrasound biopsy experience had improved procedure times and success rates when using our system.

The mean biopsy time of the inexperienced group was lower than the experienced group in both freehand and guided biopsy procedures. Participants experienced with ultrasound breast biopsy may have considered variables such as needle orientation and distance from the lesion, adding to procedure time. The inexperienced group may have proceeded with less caution, resulting in faster biopsy procedures.

A decreased procedure time of 15–20 seconds when using our system may seem insignificant; however, our results also indicated greater biopsy needle tip motion when using a freehand technique. This finding confirms the suspicions posited by Phal et al. [19], who indicated that greater procedure times would be consistent with greater needle manipulation and could result in increased tissue trauma. We attribute less needle motion to the scanning plane alignment provided by our system and the improved guidance when using the needle trajectory overlay in our graphical user interface. Participants were able to focus on the intersection of the needle trajectory overlay with the target lesion, relying less on a freehand approach for which they must intuit the intended trajectory.

The improved efficiency and accuracy yielded by use of the biopsy guidance system could lead to decreased procedure times for successful clinical biopsies of breast masses, thus reducing patient discomfort [20]. The premise of faster biopsy and reduced needle motion could reduce patient morbidity and physician apprehension to performing a technique similar to freehand biopsy.

In conclusion, breast biopsies performed on our test lesion phantom showed marked improvement with needle guidance over freehand techniques. Procedure times and needle tip movement were reduced for all participants—both inexperienced and experienced operators—when using our system. With the promise of reduced necessary experience to perform biopsy and of potentially reduced morbidity, we believe that our guidance system will enable physicians to diagnose early-stage carcinomas more efficiently and accurately.

Acknowledgments

We acknowledge the help of Lori Gardi from the Robarts Research Institute, Matt McInnis for statistical support, Kevin Barker from the University Machine Services at the University of Western Ontario, and the participants in our study: Theo Blake, Mariam Ghali, and Ashley John Mercado. We thank the following sources of funding: the Canadian Breast Cancer Research Alliance; Ontario Research and Development Challenge Fund; a Studentship provided by the Pamela Greenaway-Kohlmeier Translation Breast Cancer Research Unit; a Western Graduate Scholarship by the Schulich School of Medicine & Dentistry; and, Precarn Incorporated.

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District Court of The Hague
Corbin v Leapmed & Another

SECOND EXPERT REPORT OF
DR. RICK POPERT MS FRCS (UROL)

I, **Dr. Rick Popert**, declare as follows:

1. I am the same Rick Popert who has already provided an expert report in these proceedings.
2. In this second report, I respond to certain points raised by Prof. Debruyne in his Expert Opinion filed on behalf of the defendants to the Dutch action. I have been provided with an English translation of his opinion, which was originally filed in Dutch.
3. I do not respond to each and every point raised by Prof. Debruyne. The fact that I do not respond to a particular topic should not be taken as implying that I agree with what Prof. Debruyne has to say on the topic.

Preliminary remark

4. Before turning to a detailed discussion of what Prof. Debruyne has to say in his Opinion, I would like to make two preliminary points.
5. First, although it is occasionally unclear to me exactly what Prof. Debruyne is getting at, I do not understand him to state anywhere in his Opinion that prior art needle guides of the sort I discussed and illustrated in par. 40 of my first report had, prior to April 2014 (the priority date of the patent), been reported as being used in combination with a coaxial access needle to perform biopsies in the way which became possible with the PrecisonPoint™ device. Put simply, he correctly does not suggest that anything resembling the PrecisionPoint™ device had been disclosed prior to April 2014.
6. Nor does he state anywhere in his Opinion that he thinks such a device would have been obvious to a skilled urologist in 2014.

7. It is clear that it has proved straightforward to adapt prior art devices so that they look like the PrecisionPoint™, and possess similar characteristics or advantages. I do not believe, however, that this makes the patented PrecisionPoint™ device obvious over what went before.

8. Second, Prof. Debruyne makes much of three articles published by an Italian group in Italy who made use of coaxial needles to carry out transperineal biopsies. It is clear, however, that there is no disclosure in these articles of the use of a needle guide equipped with a coaxial needle *that was attached to a transrectal ultrasound probe*.

9. Instead, the Italian team was carrying out double free-hand biopsies, in which one hand is used to position and guide the transrectal probe, and the other hand is used to position and manoeuvre the coaxial needle and the biopsy gun. The two instruments are not attached to one another, nor indeed to anything else (such as a grid or stepper).

10. This prior art coaxial technique was difficult to perform and difficult to learn. It is quite different to the technique that is used when deploying the PrecisionPoint™ device. I will return to this point in more detail below.

Detailed discussion

<u>My experience and knowledge is not limited to the UK and my opinion is not coloured by commercial concerns</u>

11. In par. 1, Prof. Debruyne states that my experience is limited almost exclusively to the UK. This is not true. I have throughout my career kept abreast of the international literature on the diagnosis and treatment of prostate-related disease. I have also regularly published articles together with colleagues from around the world. I have a broad understanding about how prostate biopsies are carried out in mainland Europe and elsewhere. I have regularly trained colleagues in other countries, including in Ireland, Switzerland, Hong Kong, Singapore, Kuwait, Australia and New Zealand. I also taught other Dutch urologists at other urology centres. I have also taught and run training courses in the USA as part of the American Urological Association meetings.

12. Closer to home for present purposes, in 2018 and 2019 I spent a lot of time teaching and training in centres in Holland and Belgium. All of these centres were almost exclusively performing transrectal biopsies prior to their training in the PrecisionPoint™ TP biopsy techniques. An exception to the general rule was Prof. Debruyne's own private clinic (the Andros Clinic), where Jos Immerzeel, a very skilled brachytherapist, conducted MRI-directed transperineal biopsies under local anaesthetic using a stepper and grid.

13. As it happens, in 2018 I taught the PrecisionPoint™ procedure to Jos Immerzeel, who then became an enthusiastic advocate of the PrecisionPoint™ approach, which he went on to teach to other urologists operating at other centres in The Netherlands.

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14. Prior to my instructing Jos Immerzeel in the use of the PrecisionPoint™ device, I do not believe that freehand biopsies were conducted at the Andros Clinic at all[1]. Instead, Jos Immerzeel conducted, with great skill, transperineal biopsies using an MRI fusion technique which involved a stepper and grid. (That is also a technique I myself have used previously).

15. Prof. Debruyne also makes an insinuation concerning the remuneration I am paid for carrying out non-NHS training. He implies I have a conflict of interest which has affected my testimony. This too is untrue. I have always been transparent about the remuneration I receive for providing non-NHS training. I explicitly referred to this, and to my directorship at PPDT Ltd., in par. 17 of my First Expert Report. I also was obliged to declare my interests when I was appointed as a Fellow on the NHS Innovation Accelerator programme, which I did. I am also required to make an annual Declaration of Interest to my NHS employer, Guy's & St Thomas' NHS Foundation Trust, which I do.

16. As I explained in my First Expert Report, in 2019 I retired from full-time NHS practice. My commitments to the NHS Innovation Accelerator, and to the teaching and training transperineal biopsies outside of my part-time NHS contract, are carried out in my own time.

17. Prof. Debruyne goes on to suggest that my assessment is one-sided, since there are also other forms of transperineal prostate biopsy techniques which he discusses later in his report. I recognize that there are other ways of performing transperineal biopsies, and I referred to the main methods in my First Report. I have taught other methods myself: I have been training urologists to carry out transperineal biopsies since 2007, well before the introduction of the PrecisionPoint™ device.

18. My opinion as expressed in my First Expert Report reflects my experience in having carried out and taught transrectal and transperineal biopsies over the course of my 25-year career. It was my recognition of the benefits of PrecisionPoint™ biopsies that led to my involvement in the teaching and training of the technique, not because of any commercial benefit.

19. I am also familiar with the prior art techniques described by Prof. Debruyne, including the coaxial technique. In my opinion those techniques are inferior compared to the techniques enabled by the PrecisionPoint™ device, for reasons I will explain below. I prefer to teach and to practice use of the PrecisionPoint™ because I believe it is significantly better than what went before.

20. This is not just my opinion: there has been, as I explained in my First Expert Report, a wholesale shift in practice in the UK, and elsewhere, which has been brought about because of the PrecisionPoint™ device and the biopsy techniques it makes possible.

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1 I discuss the meaning of the term "freehand" below.

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The images from "*Percutaneous Image Guided Biopsy*" reproduced in Prof. Debruyne's report and the term "freehand"

21. Prof. Debruyne refers, in par. 5 and 8 of his Opinion, to a needle and ultrasound probe depicted in a chapter of a handbook entitled "*Percutaneous Image Guided Biopsy*". He reproduces the images in par. 8 of his report.

22. The ultrasound transducer and needle depicted in these figures is not, however, the kind of transducer used for carrying out prostate biopsies, nor is it suitable for such use. Instead, what is depicted is the kind of ultrasound transducer that is used for imaging the abdominal organs, such as the liver or the kidneys. The relevance of the images for prostate biopsies is not immediately apparent, but Prof. Debruyne goes on to use the images to make two points.

23. First, he says that they show that the use of an adapter mounted to a probe which is used to guide the needle has the advantage that the position of the needle is always clearly defined.

24. Second, he derives from the captions to the images a definition of "freehand" which leads him to conclude in par. 9 of his Opinion that there is a problem with claim 1 of the patent, in which a needle guide mounted onto the probe is used. He says that these are two incompatible elements: the presence of a needle guide, according to him, "*pre-eminently excludes "free-handed" biopsies*".

25. On the first point, Prof. Debruyne is being selective in his use of the literature to which he refers. On page 44 of the same chapter[2], the authors note that:

> "*Experienced radiologists prefer to use a freehand technique without a needle guide [24, 26]. The operator holds the transducer in one hand and the needle in the other. With experience, one can use either hand as the needle or operating hand and avoid crossing hands, which may lead to difficulties in orientation*"
>
> [My emphasis].

26. This passage therefore teaches *away* from using a transducer with a needle guide.

27. On the second point, I think Prof. Debruyne is using his own rather rigid understanding of the term "freehand" to try to suggest there is a lack of clarity in claim 1 of the patent. (At least: I think this is what he is trying to say, but par. 9 of his Opinion ultimately peters out, leaving it unclear what his ultimate criticism is).

28. In any event, I do not perceive the same difficulty. There may be some looseness in the use of the term "freehand" in the field, and the caption under Fig. 4.4 may or may not reflect that, but the use in the patent of the term "freehand" is consistent with my own experience of general usage in the profession and with what is said elsewhere in the literature. It simply

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2 The chapter is annexed hereto as **Exhibit RP-7**.

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means that the technique is carried out freehand, without a stepper (a stabilising device either attached to the operating table or the floor which is often used in template-grid guided biopsy approaches).

29. The term "freehand" has, in this context, a similar meaning to the use of the term in the phrase "freehand sketch". It is the clinician's hand which is freely guiding the device. "Freehand" reflects the fact that is the skill and dexterity of the clinician which allows him or her manually to move the transducer and/or biopsy needle into the correct position for taking the biopsy cores.

30. The technique used by the group in Italy discussed by Prof. Debruyne later in his report involves the use of both hands to "freehand" guide two devices (the probe on the one hand, and the biopsy needle, through the coaxial needle, on the other). This is often termed a "double freehand" technique.

31. This usage of the terms is explained in the recent article I referred to and exhibited in my First Expert Report (**Exhibit RP-6**), which was published by a large international group of urologists, myself included[3]. In the *Discussion* section in the left column of p. 315, the article states the following:

> "*The use of a TP access system is less cumbersome, flexible and painful than the brachytherapy grid [11]. These can be either probe-mounted, such as the PrecisionPoint used in this series, BK 1342/1232, Leapmed or Koelis devices, which allow a* ***single-freehand*** *technique where only the hand carrying the US can move freely; or non-fixed, such as a coaxial needle or the CamPROBE, which are used in a* ***double-freehand*** *manner where both the US and biopsy carrying hands are required to move independently [12]. Although we have not been able to undertake a detailed learning curve analysis with the available data, we believe that the single-freehand technique is easier for less experienced operators facilitating the transition from TRUS- guided biopsy. Although similar results can be achieved using a double-freehand technique, it is more difficult and can take several years [13].*"
>
> [My emphasis].

32. The use of the term "freehand" in the patent is in my view perfectly consistent with this passage, though it would have been equally correct to use the term "*single freehand*" in respect of the use of the patented device.

33. Another point emerging from the passage I quote above is that the authors (all 28 of us, from as far afield as New Zealand, Australia and Hong Kong) believed that the use of a single-

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3 Lopez JF, Campbell A, Omer A, Stroman L, Bondad J, Austin T, Reeves T, Phelan C, Leiblich A, Philippou Y, Lovegrove CE, Ranasinha N, Bryant RJ, Leslie T, Hamdy FC, Brewster S, Bell CR, Popert R, Hodgson D, Elsaghir M, Eddy B, Bolomytis S, Persad R, Reddy UD, Foley C, van Rij S, Lam W, and Lamb AD, *Local anaesthetic transperineal (LATP) prostate biopsy using a probe-mounted transperineal access system: a multicentre prospective outcome analysis*, BJU Int 2021; 128: 311–318 doi:10.1111/bju.15337 (**Exhibit RP-6** to my First Expert Report).

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freehand technique such as that using the PrecisionPoint™ device (or indeed the Leapmed device) was easier for less experienced users to learn than double-freehand techniques such as the coaxial needle technique, where both the ultrasound and biopsy carrying hands are required to move independently.

34. Ultimately, though, Prof. Debruyne's quibble on the meaning of the term "*freehand*" does not really go anywhere. It is a red herring.

The Galfano 2007 paper

35. In par. 10, Prof. Debruyne states that according to the Galfano 2007 paper, the transperineal technique offers a lower risk of infections and other complications, a higher detection rate and better sampling than the transrectal route. This is incorrect. The article actually concludes as follows:

> "*In conclusion, though having a strong rationale, the transperineal approach has not convincingly been demonstrated to provide detection rates higher than transrectal biopsy. High-quality, comparative studies must be performed to assess which kind of biopsy provides better results.*"

36. The majority of the studies reviewed by Galfano used free-hand biopsy with or without a co-axial needle. The use of the co-axial needle facilitated the fan technique by reducing the trauma caused by multiple punctures, or (where the same puncture hole was used for repeated passage of the biopsy needle) by reducing the trauma of continually re-passing the biopsy needle through the same puncture hole. Prof. Debruyne correctly does not suggest that Galfano discloses the possibility of attaching the coaxial needle (or a structure containing the coaxial needle) to an ultrasound probe. The image he reproduces in par. 19 of his report confirms that the biopsy needle was not attached to the probe: the drawing shows the probe remaining in the same position while the needle is "fanned" in different directions:

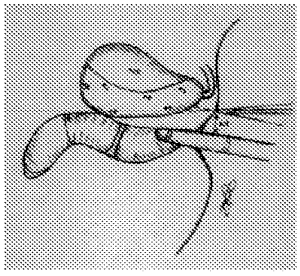


Fig. 1 - site of core sampling at the right prostate's base. Cores 1, 3, and 5 correspond to the traditional sextant biopsy protocol. Cores 7, 9, and 11 refer to the additional, peripheral, lateral sextant. Core 13 comes from the transitional zone. The coaxial needle, which allows the atraumatic passage of biopsy needle, is inserted 1.5 cm above the anal sphincter on the rectilinear line under local anaesthesia.

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37. The double-freehand coaxial techniques discussed in Galfano and the other publications from the group in Verona were, as the passage I have quoted in par. 31 above confirms, difficult to learn and to use. This is because they required the clinician to have a high degree of dexterity in both the hand that was manipulating the ultrasound probe, and the hand that was manipulating the needle. For this reason, the double-freehand coaxial technique has not been widely adopted.

38. The PrecisionPoint™, on the other hand, facilitates the targeting of the peripheral zone of the prostate (which is the tissue that is most likely to harbour prostate cancer), because the fixation of the guide to the probe keeps the needle parallel to the probe and in the plane of the peripheral zone. The possibility of fixing the guide to the probe also means that, in use, the probe can be used to manipulate and adjust the position of the prostate gland to make it possible to use just one hand to access areas of the prostate which are typically difficult to access using either transrectal techniques, or coaxial transperineal techniques.

39. Since the technique is free-hand, the practitioner is not restricted to biopsy locations dictated by a grid configuration. The practitioner can freely manoeuvre the ultrasound probe to align the access needle to target the desired locations with certainty in a strategic and parallel direction. The clamping mechanism allows the practitioner to use their existing ultrasound platform and probe (bi-planer or tri-planer linear transducer probe). Using a bi-plane or tri-planer linear ultrasound probe, one can adjust the position not only to probes of varying diameter, but also to any location along the shaft of the probe. The 15 gauge access needle snap fits into the desired aperture of the sliding carriage allowing for a multitude of samples to be taken through a single puncture of the skin.

40. The PrecisionPoint™ device, with its integrated access needle, facilitates manipulation of the prostate to meet the needle at different levels. This is achieved by simply elevating or lowering the hand holding the probe. For instance, if the access needle is pointing towards the middle of the prostate, to sample the prostate more posteriorly, maintaining the same relative axial and sagittal position, the hand holding the probe is simply elevated by 20 degrees. The prostate gland and the access needle tilt together and the trajectory of the biopsy needle is directed more posteriorly to take the biopsies. To access the anterior prostate, the hand holding the ultrasound probe is lowered towards the floor. The probe is consequently pushed against the rectal wall, compressing the prostate against the pubic arch bone. This movement flattens the prostate and tilts the prostate apex down. In this way, the trajectory of the needle can be directed towards the anterior apical prostate.

41. To sample different areas of the prostate systematically from one side to the other, the practitioner simply points the probe from medial to lateral across the prostate. The easiest way to imagine this is if the probe and device are in the midline, then the probe is pointing in the line of the patient's nose. To move across the prostate from the midline point to the lateral surface, the practitioner simply points the probe progressively in the line of the patient's ear, the clavicle and the shoulder. Because the needle guide is held by the

PrecisionPoint™ Access System in the line of the probe, different areas of the prostate from side to side and up and down can be accessed through a single puncture, within the plane of the peripheral zone.

42. This control of needle trajectory is considerably more difficult to achieve consistently using the double-freehand co-axial fan technique, and virtually impossible with the restrictions afforded by grid-based biopsy systems, including the BK UA 1234 discussed below, where multiple apertures require multiple punctures to access different areas of the prostate.

43. The degree of leverage and control of needle trajectory is in my experience the most unique and important feature of the PrecisionPoint™ device, differentiating it from any other biopsy device or system that were available prior to April 2014 (the priority date of the patent).

The BK UA1324

44. In par. 15 to 16, Prof. Debruyne discusses the BK UA 1234 guide with multiple apertures. This device was used to take biopsy cores one above the other, in much the same way as in a grid-based biopsy.

45. Prof. Debruyne refers in par. 16 to the *rotation* of the probe about its longitudinal axis to take a second column of biopsies. Rotation, however, necessarily implies the making of multiple punctures, since the probe, with the needle guide (and needle) attached to it, is being rotated into different positions. This cannot be done if the needle is in the perineum. The needle must be removed from the perineum and then replaced in another hole and passed into the perineum repeatedly.

46. This is a critical difference with PrecisionPoint™, where the access needle remains in the perineum, held by the device in the line of the ultrasound transducer. By pointing the ultrasound probe from medial to lateral, biopsies can be taken from different areas. By tilting the hand up or down, the prostate can be moved to meet the needle at different levels without having to remove the access needle.

47. Prof. Debruyne correctly does not assert in his Opinion that there is any disclosure, prior to 2014, of using the BK UA 1234 device with a coaxial introducer needle inserted in the needle guide.

Onik's patent application

48. In par. 18 of his report. Prof. Debruyne refers to Onik's patent application. This application refers to a needle guide used to place biopsy needles and cryotherapy needles through the perineum into the prostate. The summary describes that "*This structure provides a needle insertion guide which can be mounted on a rectally inserted ultrasound guide used to image a prostate. The insertion guide will rotate relative to the patient when the ultrasound probe is rotated about its longitudinal axis and the slide block is adjustable along the adjustment guide to alter the radial distance of the needle holder and guide from the ultrasound probe*".

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49. In this manner, the entry position of the needle and its position of placement within the prostate is adjustable in an anterior-posterior dimension by adjustment of the slide block position, as well as by rotating the ultrasound probe.

50. The needle insertion guide can be moved in an anterior – posterior dimension, effectively replicating the multiple levels of a grid, but not being restricted to a fixed distance. Importantly, however, the summary goes on to state the following:

> "*In addition, the needle holder and guide assembly is adjustable relative to the slide block in a direction parallel to the longitudinal axis of the ultrasound probe in order to engage the perineum of the patient and thereby stabilize the instrument*".
> (My emphasis).

51. It is therefore clear that the needle guide is being used here to engage the perineum in order to stabilize the instrument. The needle guide is not entering the perineum. Again, there is no disclosure of an access needle in the sense of Corbin's patent.

Prof. Debruyne's remaining criticisms of my testimony

52. In par. 23 to 30, Prof. Debruyne criticizes what I said in my First Expert Report about prior art methods of taking biopsies. The comments in my First Expert Report related to biopsy procedures being used prior to 2014. I accept that template mapping or saturation biopsies of 50 or more cores are performed less frequently nowadays, but they were often performed then.

53. Prof. Debruyne's description of MRI-targeted biopsies with 10 – 12 systematic cores using a grid on a stepper is a technique which can indeed be carried out, by highly skilled practitioners, under local anaesthetic. This was a technique that was, for example, as I have noted above, being carried out at Prof. Debruyne's own private clinic by his colleague Jos Immerzeel.

54. This does not, however, cover the majority of cases in the majority of centres, where such techniques are poorly tolerated under local anaesthetic. Many patients will require sedation or general anaesthesia, because the probe on the stepping unit is uncomfortable and the technique still requires multiple perineal punctures. For these reasons, until the PrecisionPoint™ was introduced, the overwhelming majority of transperineal grid-based biopsies were performed under general anaesthesia.

55. Prior to 2014, patients were offered a transrectal ultrasound biopsy by default. In most hospitals that were able to offer transperineal biopsies as an alternative, this was not usually offered as a first line service, unless imaging had demonstrated an anterior tumour. Hospital Episode Statistics data in the UK for 2014 – 2015 showed that transperineal biopsies accounted for only 20% of all prostate biopsies. Almost all of these were under general anaesthetic. Without providing any data of his own, Prof. Debruyne criticizes me for not discussing the situation in mainland Europe, but I suspect, based on my discussions with

Dutch colleagues, particularly in the 2018 – 2019 period, that the situation in The Netherlands was even worse than it was in the UK, with probably over 95% of biopsies being transrectal.

56. Prof. Debruyne refers to a 2013 comment of Peter Acher as reflected in an editorial of the BJU International as suggesting that a perineal biopsy under local anaesthetic was possible. As it happens, Peter Acher worked with me and was trained in grid-based transperineal biopsies. He witnessed at first hand our own attempt at Guy's Hospital to carry out local anaesthetic OPD grid-based transperineal biopsies. As I explained in my First Expert Report, although the technique was feasible, it was not practical. It was tolerable rather than comfortable. After experimenting with transperineal biopsies under local anaesthetic, we ultimately reverted to transperineal biopsies under general anaesthesia. That situation continued up until the PrecisionPoint™ biopsy was introduced.

57. In par. 29 Prof. Debruyne takes issue with what he says is *my view* of what happened in the UK. In fact, this is not my view, but a reflection of NHS Hospital Episode Statistic (HES) Data. The data confirmed that by April 2021, transperineal biopsies now account for 65% of all prostate biopsies. Data from BXTA indicate that over 80% of these transperineal biopsies are done using the PrecisionPoint™ device.

58. Finally, Prof. Debruyne returns, in the last paragraph of his Opinion, to Galfano and Ficarra, and says that my description of the use of the PrecisionPoint™ device essentially corresponds to the fan technique described by them. This statement is simply wrong. As I have explained above, the PrecisionPoint™ device keeps the access needle in the plane of the peripheral zone of the prostate *and* in the longitudinal plane of the ultrasound probe. The double freehand "fan" technique does neither. Instead, one hand has to steer the needle, and the other hand has to hold the ultrasound probe in-line with the needle. The fan technique is complicated to learn and cumbersome in operation. The PrecisionPoint™ device is neither.

59. It is in my opinion telling too that, despite Prof. Debruyne's championing of the fan technique in his Expert Opinion, his own private clinic does not, as far as I am aware, make use of the fan technique, either with or without a coaxial needle. Instead, as I have explained above, his clinic makes use of a grid-based MRI fusion targeted technique to take prostate biopsies under local anaesthetic. This technique involves the use of a grid to make multiple punctures in the perineum.

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Statement of truth

60. The facts stated in this report are true to the best of my knowledge and belief and the opinions stated herein are truly held. What is set out above is based on my own knowledge and experience and represents my complete and professional opinion. I am prepared to attend Court and confirm the contents of this expert report under oath.

Signed: // Rick Popert //

Dr. R. Popert

on this 15th day of November 2021

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District Court of The Hague
Corbin v Leapmed & Another

WITNESS STATEMENT OF
DR. MATTHEW J. ALLAWAY

I, Dr. Matthew J. Allaway declare as follows

Background

1. I am a urologist. In 1996 I graduated from the Chicago College of Osteopathic Medicine, and subsequently received my qualifications at the West Virginia University where I completed my residency in General Surgery in 1998, and my residency in Urology in 2002. After my residency, I moved to Maryland where I set up a specialised urology practice, Urology Associates. I have been practicing there for almost 20 years now.

2. A special focus of my practice is prostate cancer.

3. As I explain below, driven by the clinical and technical challenges that I encountered in the practice of taking prostate biopsies, I developed the PrecisionPoint™ Transperineal Access System. I am the named inventor on the patent EP 3 125 811 B1 that is at issue in the present Dutch proceedings. I am also the founder and president of Corbin Clinical Resources Inc. of which Corbin Clinical Resources LLC (Corbin) which holds the intellectual property to my invention.

My instructions

4. I have been asked by Dutch counsel to explain how conventional prostate biopsies were carried out prior to the invention, and what led me to inventing the PrecisionPoint device. I understand that my statement will be relied on in the Dutch proceedings and I confirm that what is set out here is true to the best of my knowledge and belief and that the opinions expressed herein are truly held. I am prepared to confirm the contents of this statement under oath.

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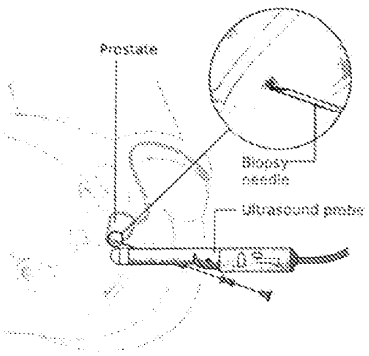
5. Prior to preparing this report, I was provided with Pelvitec's statement of defence and exhibits, including the expert report by Prof. Debruyne. In discussing my invention, I will also provide some comments on these materials. The fact that I do not respond to every single point should not be taken to mean that I agree with those undiscussed points: that is not the case.

6. I have also read Dr. Popert's First and Second Expert Reports. I agree with what he has set out there.

The difficulties with existing biopsy techniques at the priority date

Transrectal biopsies

7. In the US, but also globally, at the priority date the most commonly used technique for taking a prostate biopsy was via the transrectal route, with ultrasound imaging to help position the biopsy needle. For the transrectal approach, it was common to use a biopsy needle guide fitted to the probe, as illustrated in the image below taken from Dr. Popert's report.



8. The transrectal approach had a number of advantages. It could be carried out with a handheld probe, was easy to perform for a moderately skilled urologist, and could be carried out under local anaesthesia.

9. The two main disadvantages of the transrectal approach are complications and missed cancer. Up to 7% of patients will suffer an infection and approximately 3% will require hospitalization due to sepsis[1]. Other complications include profuse rectal bleeding. These complications are a result of passing the biopsy needle through the rectal wall to sample the prostate. At least 12 separate punctures through the rectal wall are needed for this biopsy The second major disadvantage is the difficulty in sampling the entire prostate. The anterior and apical prostate (more than 20% of cancers found) are typically missed with the transrectal biopsy due to anatomical limitations when passing the biopsy needle through the rectum.

[1] Ristau et al, "Free-hand transperineal prostate biopsy provides acceptable cancer detection and minimizes risk of infection: evolving experience with a 10-sector template", Urol Onc 2018, 36(12) (**Exhibit MA-1**)

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Transperineal biopsies

10. Transperineal prostate biopsy techniques were also known and in use well before 2014. For the pre-priority techniques, a distinction may be made between the techniques that used a template to guide the biopsy needle, and those that did not.

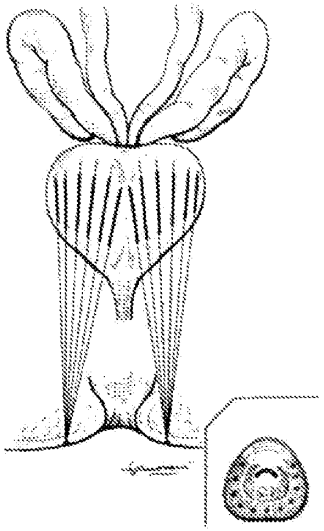
11. Dr. Popert has already described the approaches that use a template or grid in his first report.

12. Using a grid/template approach, the biopsy trajectory is determined by the grid hole and not the geometrical configuration of the zones of the prostate where prostate cancer originates. Thus, one will often need to take three biopsies to cover a region of interest. In addition, for each biopsy sample taken, the biopsy needle traverses through the skin, subcutaneous tissue, and the prostate. A significant number of samples would be needed to sample the entire prostate, necessitating an equal number of perforations of the perineum. Although the cancer detection is optimal, the procedure requires general anesthesia and significant resources of the operating theater. Since the prostate biopsy is performed on over 3 million men worldwide each year, this is not a suitable approach for mainstream adoption.

13. The second category of transperineal techniques did not use a guide for the needle at all. Instead, the urologist would manoeuvre an ultrasonic probe with one hand, and with the other hand would independently manoeuvre the biopsy needle. This requires a high degree of skill and dexterity on the part of the clinician. It is a technique which has a long learning curve and is relatively difficult to master.

14. The defendant in this case have provided a number of publications from an Italian group that used the so-called "fan technique" for transperineal biopsies. In the fan technique, the biopsy needle is inserted several times through the same skin puncture, each time at a different angle. I have reproduced below an illustration from a 2001 paper by an Italian group that illustrates this[2] (**Exhibit MA-2**).

[2] Emiliozzi et al, "*The value of a single biopsy with 12 transperineal cores For detecting prostate cancer in patients with elevated prostate specific antigen, Journal of Urology*", Vol. 166, pp. 845–850, September 2001. This article is reference [21] to Galfano's 2007 article, exhibit GP29 of the defendants.



15. It was subsequently recognized that patient comfort could be improved by keeping the access point open using a coaxial needle. This is what is described in the articles by the Italian team in Verona (Ficarra, Galfano and Novella) that Pelvitec referred to in the Dutch proceedings. The advantage of carrying out the biopsy in this way is that the use of the coaxial needle means that the biopsy needle causes less trauma than repeatedly pushing the biopsy needle through the same perforation.

16. It should be noted that in the techniques discussed in these articles, the coaxial needle is always manipulated independently of the probe. This remains, therefore, a procedure in which the urologist must manoeuvre the probe with one hand, and independently manoeuvre, using his other hand, the biopsy needle passing through the coaxial needle.

17. This is sometimes described as a "*double free-hand*" approach. Each hand is acting freely, without being guided by a template, and without the device that is held in one hand being attached to the device that is held in the other. This is a difficult manoevre and slightly de-synchronous movements often lead to the loss of vision of the biopsy needle on the ultrasound screen.

18. The free-hand "fan-technique" has been around for nearly 20 years. Prior to development of the PrecisionPoint™ prostate biopsy, I used this approach myself. This method certainly had some benefits over the transrectal biopsy due to avoidance of the fecal bacteria. However, there was notable limitations that could not be overcome. First, though multiple biopsies could indeed be taken via a single access point, it was often still needed to make multiple punctures in the perineum to properly sample the anterior/apical prostate. In addition, the cancer detection was suboptimal compared with the grid/template transperineal biopsy. The technique was also challenging for the urologist to learn because of the need to

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monitor the ultrasound probe separately from the biopsy gun. Thus, standardization and reproducibility were seriously lacking.

19. With the double free-hand approach, I found that it was almost impossible to separate each biopsy from subsequent cores. The biopsy needle typically passes through the zones of the prostate where cancer does not originate, and it was not possible to keep the biopsy needle entirely in the relevant zones of the prostate. Other urologists that I attempted to train were often unable to reproduce the method because they could not properly coordinate manipulating the probe with one hand guiding with the second hand the biopsy gun into the target. As a result, many of these urologists were getting a cancer detection that was even lower than the results obtained with the transrectal technique.

What did not exist: a device that combines the benefits of a needle guide and the freehand technique with only one or two access holes by using a coaxial needle

20. Faced with the difficulties of existing techniques, I realised there was a need for a new device which would allow for the benefits of the two different approaches for transperineal biopsies that existed at the priority date to be combined. I therefore developed the PrecisionPoint™. This device offers the precision of a needle-guided technique, and the patient comfort of a freehand fan technique. The typical disadvantages associated with both prior art techniques are obviated with the PrecisionPoint™: it requires no expensive, cumbersome stepper, no general or spinal anaesthesia, and the technique using the device is straightforward to carry out and straightforward to master.

21. I started working on trying to solve this problem and to come up with a device and method that would encourage the adoption of the transperineal approach. My goals was to make a device that:

(i) achieve a cancer detection comparable to the grid/template;

(ii) can be used under local anesthesia; and

(iii) can be used with the resources commonly in use for a transrectal biopsy.

22. During the development process, I came to understand that key to the solution is to anchor an access needle into the perineum with the stability to withstand the counter forces of the anatomy as the access needle is shifted to various positions in the x,y and z coordinates. With such a device, the biopsy trajectories will not simply be fanned, but instead re-positioning the exit-point of the access needle to a unique and definable point to access the most relevant zones of the prostate for ideal cancer detection. Another key element in my mind was that the device should also be coupled to the ultrasound probe so the biopsy needle trajectory can be constantly monitored. To arrive at the PrecisionPoint™, I designed over two dozen iterations using CAD engineers and 3D printed parts. It is the combination of the needle guide, equipped with a coaxial needle, which needle guide can be fixed to the