

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

EMBODY, INC. AND ZIMMER BIOMET HOLDINGS, INC.,
Petitioner

v.

LIFENET HEALTH,
Patent Owner.

Case No. IPR2025-00249
U.S. Patent No. 11,318,227

PATENT OWNER'S PRELIMINARY RESPONSE
37 C.F.R. § 42.107(a)

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LIST OF EXHIBITS

Patent Owner's Exhibits

Exhibit Number	Description
2001	U.S. Patent Application Publication No. 2012/0221025, published Aug. 30, 2012 (“Simpson”)
2002	WO 2012/078472, published June 14, 2012 (“Patel”)
2003	Dorland’s Illustrated Medical Dictionary (29th ed. 2000) – “progenitor”
2004	Dorland’s Illustrated Medical Dictionary (29th ed. 2000) – “stem c[ell]”

I. INTRODUCTION

Patent Owner LifeNet Health (“LifeNet” or “Patent Owner”) submits this Preliminary Response to the Petition for *Inter Partes* Review filed by Embody, Inc. and Zimmer Biomet Holdings, Inc. (“Petitioner”), by which Petitioner challenges claims 1–8 of U.S. Patent Number 11,318,227 (“the ’227 patent”). Paper 2 (“Petition” or “Pet.”).

Patent Owner respectfully requests that the Board deny the Petition for at least two reasons: (1) Petitioner fails to demonstrate that the prior art teaches or suggests “a result of a fast Fourier transform (FFT) analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other,” as recited in each challenged claim,¹ and (2) Petitioner fails to demonstrate that it would have been obvious to combine the asserted prior art.

First, Petitioner fails to meet its burden to demonstrate a reasonable likelihood of prevailing under 35 U.S.C. § 314(a). Petitioner presents three grounds of unpatentability, each relying upon either Huang² or Lee³ as its primary reference.

¹ Challenged independent claims 1 and 7 each recite this limitation, except claim 1 recites “fast Fourier transform (FFT) analysis” while claim 7 recites “FFT analysis.”

² Huang et al., *The involvement of integrin β 1 signaling in the migration and myofibroblastic differentiation of skin fibroblasts on anisotropic collagen-containing nanofibers*, 33 BIOMATERIALS 1791–1800 (2012) (“Huang2,” Ex. 1005).

³ Lee et al., U.S. Patent Application No. US 2010/0331980 A1, published Dec. 30, 2010 (“Lee,” Ex. 1011).

However, Petitioner does not assert that *either* primary reference presents a “result of a FFT analysis” with “major adjacent peaks that are about 180° apart from each other.” Petitioner could not make such an assertion credibly: Petitioner and its expert admit that Huang² discloses a FFT analysis result with one single peak, and Lee does not disclose FFT at all. Pet. 28; Ex. 1003 ¶ 120; Ex. 1005, 1793;⁴ Ex. 1011.

Instead, Petitioner impermissibly relies on its expert to provide this missing limitation. In doing so, however, Petitioner and its expert studiously avoid the actual claim language and instead present inapposite arguments about “aligned” fibers. *See, e.g.*, Pet. 35, 47, 60. But the claims do not recite “aligned” fibers; they recite a specific “result of a FFT analysis” that has “major adjacent peaks that are about 180° apart from each other.” Petitioner fails to demonstrate that “aligned fibers” is the claimed FFT analysis result.

Second, Petitioner’s obviousness grounds fail to reckon with important differences between the cited references, which are essential to each reference’s ability to repair tissue defects. Huang², Lee, and Kuo⁵ teach scaffolds seeded with different, particular cells to promote repair of different, particular tissues. Ex. 1005,

⁴ For consistency with Petitioner’s briefing, Patent Owner cites to exhibits’ native page numbering.

⁵ Kuo et al., U.S. Patent Application No. US 2011/0293685 A1, published Dec. 1, 2011 (“Kuo,” Ex. 1018).

1799 (skin); Ex. 1011 ¶ 72 (muscle); Ex. 1018 ¶¶ 16 (tendon), 58 (various other tissues). Petitioner fails to demonstrate that a skilled artisan would have been motivated to treat a tendon tissue defect, for example, with a scaffold embedded with skin or muscle cells, or would have expected success in doing so. Such a suggestion defies common sense.

Patent Owner respectfully requests that the Board deny institution.

II. THE '227 PATENT

A. The '227 Patent

1. A scaffold comprising electrospun fibers

The '227 patent discloses a “scaffold comprising an aligned fiber.” Ex. 1001, Abstract, 13:23–29. This scaffold may be used to facilitate growth of, for example, bone, ligament, or tendon tissue, *id.* at 11:28–57, and may be incorporated into biocompatible implants used for, e.g., “repairing or restoring tissues damaged by disease or trauma.” *Id.* at 16:18–20. “The invention also relates to methods of treating a tissue or organ defect or injury, for example, a musculoskeletal, dental or soft-tissue defect or injury, in an animal comprising administering ... the aligned fiber, electrospun fiber, scaffold and/or implant described herein to the tissue or organ defect (e.g. osseous defects, defects in cartilage, ligament, tendon, spinal disk, and tendon insertion site to bone).” *Id.* at 18:54–62, 16:53–17:5 (nerve repair).

The '227 patent discloses that scaffolds comprising aligned fibers may be formed by electrospinning. *Id.* at 13:23–25. Through electrospinning techniques,

fibers may be formed “as small as one nanometer.” *Id.* at 2:42–44. The ’227 patent discloses embodiments where electrospun fibers are aligned in one direction and may be formed into an elongated roll, elongated sheets, a composite of multiple layers of sheets, or a combination thereof. *Id.* at 8:26–35. The ’227 patent further explains that these scaffolds may comprise collagen. *Id.* at 13:50–14:2.

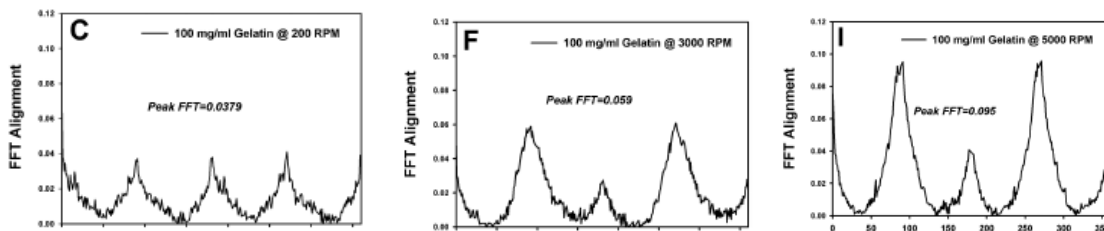
2. Fast Fourier transform analysis

To measure alignment of the scaffold’s fibers, the ’227 patent employs a fast Fourier transform (“FFT”) analysis. *Id.* at 13:38–49. This technique is further described in a 2008 publication, to which Petitioner’s declarant Dr. David G. Simpson is the senior author, and which the ’227 patent incorporates by reference. *Id.*; Pet. 11; Ex. 1003 ¶ 62.⁶

Dr. Simpson’s 2008 paper describes using FFT analysis “to measure fiber alignment in electrospun materials.” Ex. 1010, Abstract. With this approach, “[t]he 2D FFT function converts spatial information in an optical data image into a mathematically defined frequency domain,” which “maps the rate at which pixel intensities change in the spatial domain.” *Id.* at 608.

⁶ Petitioner refers to two of Dr. Simpson’s papers as the “Ayres” papers because Chantal E. Ayres is the first-named author. Ex. 1010; Ex. 1013; *see, e.g.*, Pet. 11. However, Dr. Simpson is listed as a co-author on each paper, and Petitioner states that Dr. Simpson is the “senior author” of the 2008 paper. Pet. 11; Ex. 1003 ¶ 62. For clarity in recognizing the relationship between Petitioner’s declarant and these papers, Patent Owner refers to them as Dr. Simpson’s papers.

Dr. Simpson's 2008 paper provides three examples of the results of a FFT analysis, shown below.



Ex. 1010, 608 at Figs. 1C, 1F, 1I. Each figure depicts FFT alignment plotted on a scale from 0 to 360°. *Id.*

Consistent with these figures, Dr. Simpson's 2008 paper explains that a FFT analysis result for "a random matrix will exhibit 4 peaks that occur every 90°. Peaks of nearly uniform height are a hallmark of a scaffold composed of random elements." *Id.* at 609, Fig. 1C. By contrast, "plots generated from sample scaffolds containing aligned elements exhibit asymmetrical peaks, two larger peaks at 90 and 270° and two smaller peaks at 0 and 360° (Fig. 1F and I)." *Id.* at 610.

Dr. Simpson's 2008 paper explains that a FFT analysis result conveys several pieces of information. For example, "the height and overall shape of the most prominent peaks present in the alignment plot" conveys "[t]he degree of alignment present in the original data image." *Id.* (emphasis added). Additionally, the shape of the peak conveys the uniformity of fiber alignment, where "[a] high and narrow peak indicates a more uniform degree of fiber alignment, [but] a broad peak, or a shoulder on the peak indicates that more than one axis of alignment may be present."

Id. (emphasis added). Finally, “the principal axis of fiber alignment is determined by the position of the alignment peaks,” e.g., in the vertical direction in Figures 1F and 1I above. *Id.* (emphasis added); *see also* Ex. 1003 ¶¶ 41–42 (explaining that a FFT analysis result “reflects the directional orientation of the fibers,” “provid[es] a visual summary of the[] orientation,” and “illustrates the degree of fiber alignment”).

Similarly, the ’227 patent explains that the FFT analysis result of the claimed scaffold with electrospun fibers shows “adjacent major peaks with about 180° apart from each other,” where “major peaks” “refer to peaks higher than the average of the peaks in the result.” Ex. 1001, 13:25–29. This is depicted in Figure 8A of the ’227 patent, reproduced below alongside Figure 8B.

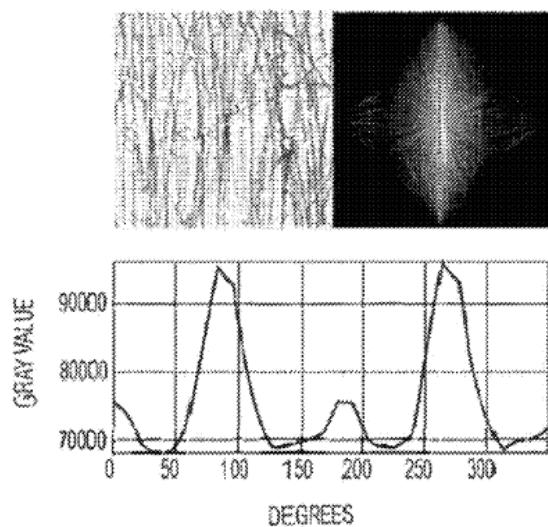


FIG. 8A

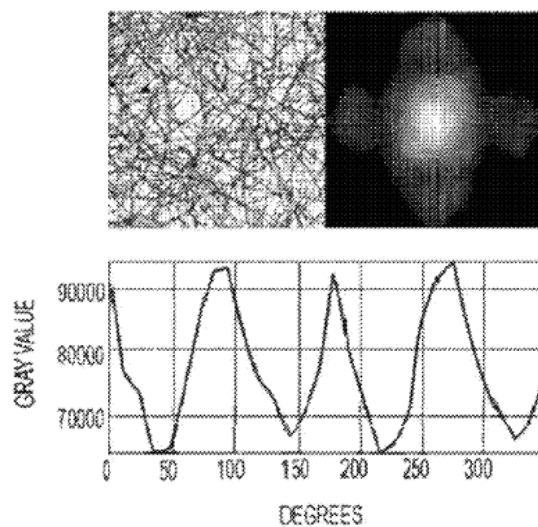


FIG. 8B

Id. at 13:46–49, Figs. 8A–8B. “FIG. 8A depicts exemplary FFT analysis results of the fibers described herein ... Fig. 8B depicts an FFT analysis of a control sample.”

Id. at 2:10–12. As shown, the FFT analysis result in the '227 patent is plotted between 0° and 360°, where aligned fibers described in the '227 patent show adjacent major peaks with about 180° apart from each other (Figure 8A), and where non-aligned fibers do not (Figure 8B). *Id.* at 13:46–49.

3. Cell seeding

Finally, the '227 patent discloses that cells may be seeded and cultured on the scaffold. *Id.* at 10:56–57, 16:26–27. “In some embodiments, the cells are selected from ... stem cells, adipose derived stem cells, dental pulp stem cells, fibroblasts, and dorsal root ganglia.” *Id.* at 16:27–30, 16:43–52 (describing conditions). The '227 patent explains that “differentiation of stem cells into osteoblasts, chondrocytes, ligament or tendon” may be promoted by “culturing the cells on the scaffold or aligned fiber described herein in conditions suitable for the cell differentiation.” *Id.* at 1:31–35, 16:54–18:17.

B. The '227 Patent Claims

Of the '227 patent's 14 issued claims, only claims 1–8 are challenged in the Petition. Pet. 1. Of those, claims 1 and 7 are independent and recite:

1. A method of treating a tissue defect in a subject comprising[:]
implanting at the tissue defect a scaffold comprising crosslinked fibers comprising collagen, wherein a result of a fast Fourier transform (FFT) analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other, and
applying the scaffold to the tissue defect to repair a tendon, a ligament or a nerve defect.

7. A method of cell culture comprising[:]

placing cells on a scaffold comprising aligned fibers, wherein a result of a FFT analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other, and growing the cells in conditions suitable for the cell culture.

Ex. 1001, 23:29–37, 24:5–11.

C. Prosecution of the '227 Patent

U.S. Patent Application No. 16/045,159 (the “’159 application”) was filed on July 25, 2018, and ultimately issued as the ’227 patent. Ex. 1001, codes 21–22. The ’159 application is a divisional of U.S. Patent Application No. 14/776,106 (“the ’106 application”), now U.S. Patent No. 10,137,223,⁷ which is the national stage of PCT Application No. US2014/025636, filed March 13, 2014, and which claims priority to U.S. Provisional Patent Application No. 61/785,031, filed on March 14, 2013. *Id.* at codes 60, 62. The ’159 application was filed with 24 claims, which were cancelled in a preliminary amendment and replaced with new claims 25–35. Ex. 1002–1, 1–4.

Petitioner’s summary of the prosecution history of the ’159 application is incomplete. *See* Pet. 16–20. Petitioner alleges that prosecution “focused primarily on 35 U.S.C. § 112, with the Examiner rejecting the presented claims as both

⁷ U.S. Patent No. 10,137,223 is challenged by Petitioner in IPR2025-00248.

indefinite and non-enabled.” Pet. 19. The Examiner did issue rejections based on § 112, on December 24, 2020 (*see* Ex. 1002–2, 488, 491–497) and on July 19, 2021 (*id.* at 529, 532–537). However, as part of the July 19, 2021, Office Action, the Examiner also rejected pending application claim 26 under 35 U.S.C. § 102(b) as anticipated by prior art that is substantially the same as that presented in the Petition. *Id.* at 537–538.⁸

Specifically, the Examiner rejected application claim 26 as anticipated by Simpson,⁹ which the Examiner found taught “construction of fibrous scaffolds (see e.g. ¶0035) which is anisotropic (see e.g. ¶0011). The fibers comprise collagen (see e.g. 0049). These are used to repair nerve damage (see e.g. abstract). The fiber anisotropy is measured using Transform analysis (see e.g. ¶0100).” *Id.* at 538.

The Examiner also rejected claim 26 as anticipated by Patel,¹⁰ which the Examiner found taught “construction of fibrous scaffolds with collagen (see e.g. ¶0189) which is anisotropic (see e.g. ¶0323). These are used to repair tendon,

⁸ The Examiner also issued an obviousness-type double patenting rejection over U.S. Patent Application No. 16/989,307. Ex. 1002–2, 538–539.

⁹ U.S. Patent Application Publication No. 2012/0221025, published Aug. 30, 2012 (“Simpson,” Ex. 2001).

¹⁰ WO2012/078472, published June 14, 2012 (“Patel,” Ex. 2002).

ligament or nerve damage (see e.g. ¶0168). As evidenced above, the fiber anisotropy is measured using Fourier Transform analysis.”¹¹ *Id.*

After the Examiner’s rejections, the applicant cancelled application claim 26, among others, and amended several pending claims. *Id.* at 648–650 (claims), 651. The applicant also argued against the Examiner’s enablement rejection. *Id.* at 652–653.

The applicant and Examiner conducted an interview on February 8, 2022, *id.* at 662–663, and the Office allowed the ’159 application thereafter, which issued as the ’227 patent on February 28, 2022. Ex. 1002–2, 664–670.¹²

III. LEVEL OF SKILL IN THE ART

At this stage of the proceeding, Patent Owner does not raise a dispute regarding Petitioner’s identified level of skill possessed by a person of ordinary skill in the art (“POSITA”). Pet. 20–21.

IV. CLAIM CONSTRUCTION

At this stage of the proceeding, Patent Owner does not raise a dispute regarding Petitioner’s assertion that claim construction is not necessary. Pet. 21.

¹¹ The Examiner’s rejection mistakenly referred to Patel as “Yeo et al.” Ex. 1002–2, 538. The Examiner clarified that the reference to “Yeo” was incorrect. *Id.* at 636.

¹² Minor amendments were made after allowance to correct a typographical error. *Id.* at 685–691 (deleting “and ,”; adding --and-- in application claim 25).

V. PETITIONER FAILS TO PRESENT A REASONABLE LIKELIHOOD OF UNPATENTABILITY FOR ANY CHALLENGED CLAIM

A. Petitioner's Assertions of Unpatentability

1. The Asserted Grounds

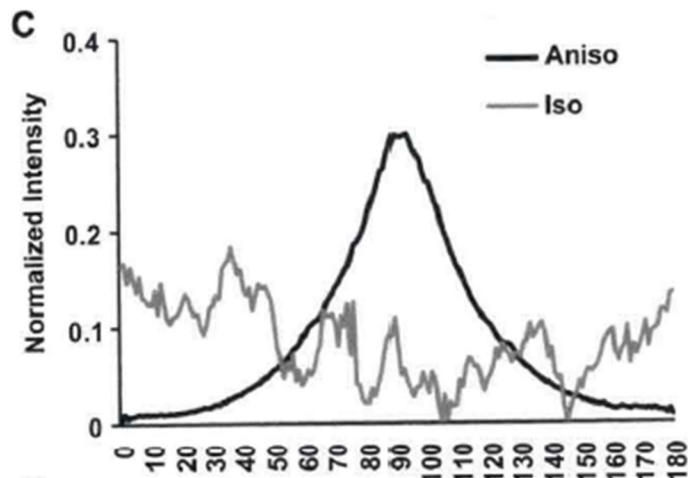
Petitioner asserts that claims 1–6 are obvious under 35 U.S.C. § 103 by (1) Huang2 and Kuo; or (2) Lee alone, or with Kuo; Petitioner also asserts that claims 7–8 are anticipated under 35 U.S.C. § 102 by Huang2. Pet. 4.

2. The Asserted Prior Art

a) Huang2

Huang2 discloses scaffolds for skin tissue repair. Ex. 1005, Abstract (“skin wound repair”). Huang2 explains that, “[t]o better support and facilitate skin cells to form skin-like tissues, it is necessary for the temporary scaffolds not only to provide a surface for the cells to reside, but also to define a cell-friendly microenvironment that maximally recaptures the native extracellular matrix (ECM).” *Id.* at 1791. To best mimic the ECM, Huang2 provides an electrospun scaffold made from a blend of collagen and polycaprolactone (PCL). *Id.*

Huang2 discloses that “[t]he orientation of electrospun nanofibers was determined by using the ImageJ program (NIH) along with the Oval Profile Plot plugin.... These cropped images were then processed with a fast Fourier transform (FFT).” *Id.* at 1792. Huang2’s Figure 1C is reproduced below.



Huang2’s Figure 1C depicts “[n]ormalized intensity plots against the angle of acquisition for isotropic and anisotropic nanofibrous matrices,” plotted from 0°–180° degrees, where the anisotropic fibers have a single peak.¹³ *Id.* at 1793. Huang2 explains that “[t]he narrow peak ... in anisotropic matrices (Fig. 1C) indicated that PCL/Coll nanofibers aligned along a single axis (Fig. 1B). In contrast, the lack of significant peak for the fibers collected on a stationary surface demonstrated no preferred fiber orientation in the isotropic matrices (Fig. 1C).” *Id.* at 1794.

To facilitate skin repair, Huang2 additionally discloses that fibroblast cells are “seeded on the nanofibrous matrices” and cultured for up to 7 days. *Id.* at 1792. Huang2 reports that “NHDFs [normal human dermal fibroblasts] cultured on anisotropic PCL/collagen nanofibers showed elongated cell morphology, distinct

¹³ Huang2 defines “isotropic” as “fibers collected randomly with no alignment” and “anisotropic” as “fibers collected with alignment.” Ex. 1005, Abstract.

distribution of focal adhesions, accelerated cell migration and promoted fibroblast-to-myofibroblast differentiation.” *Id.* at 1799.

b) Lee

Lee discloses scaffolds for muscle tissue repair. Ex. 1011 ¶ 2 (“The present invention ... involves the engineering of muscle tissues.”). Lee explains that “it is preferable to mimic native skeletal muscle construction, with its highly-oriented fibers of fused mononucleated muscle cells.” *Id.* ¶ 4. To that end, Lee discloses “muscle implants including: a biodegradable scaffold comprising a plurality of fibers oriented along a longitudinal axis of the fibers; and mammalian myotubes in said scaffold and oriented along said longitudinal axis of the fibers.” *Id.* ¶ 5. The scaffold may be formed by electrospinning collagen, optionally with other synthetic polymers like PCL. *Id.* ¶ 6.

Lee does not disclose FFT analysis. Lee examines the scaffolds with, e.g., scanning electron microscopy, “ImageTool 3.0” freeware, and tensile testing. *Id.* ¶¶ 65–67.

To facilitate muscle tissue repair, Lee discloses that human skeletal muscle cells are seeded on the scaffold. *Id.* ¶¶ 72–73; *see also id.* ¶¶ 60. After being cultured on the scaffold, “[t]he cells fused and formed myotubes.” *Id.* ¶ 82.

c) Kuo

Kuo discloses scaffolds for “tissue regeneration, enhancement, or tissue

repair.” Ex. 1018, Abstract. Electrospinning may be “used to create mats comprised of fibers that can be seeded with cells and subsequently rolled into a desired shape/form to replace a desired tissue.” *Id.* Kuo explains that “[t]hese scaffolds physically resemble the nanofibrous features of the extracellular matrix.” *Id.* ¶ 4.

Kuo teaches repair of various types of tissue depending upon the cell type seeded on the scaffold. *Id.* ¶ 58 (“[D]ifferent cell types or combinations thereof may be employed ... depending upon the intended function of the tissue engineered construct being produced.”). For example, Kuo discloses repair of ligaments, tendons, connective tissue, nerves, nerve channels, liver, pancreas, endothelial tissue, gastrointestinal tissue, cardiac tissue, ducts, bile ducts, spine discs, cranial tissue, dura, kidney, bladder, spleen, cardiac muscle, skeletal muscle, breast tissue, cartilage, and bone. *Id.* ¶¶ 52, 67–68; *see also id.* ¶ 16 (disclosing cell types).

Kuo does not disclose FFT analysis.

B. Ground 1: Petitioner Fails To Show Obviousness of Claims 1–6 Over Huang² and Kuo

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). This burden never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

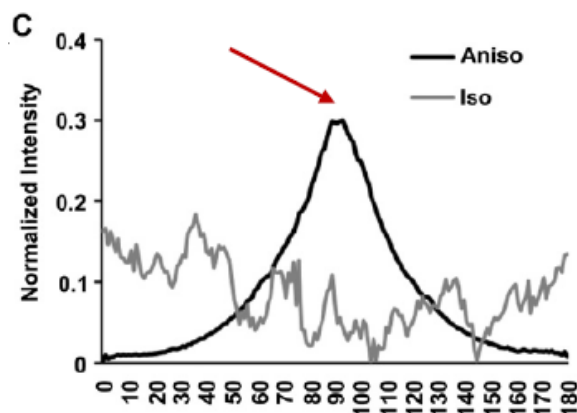
Petitioner fails to meet its burden because (1) Huang² does not teach or

suggest “a result of a FFT analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other,” (2) neither Huang2 nor Kuo teach or suggest crosslinked fibers, and (3) a POSITA would not have been motivated to modify the references.

1. Huang2 does not teach or suggest the claimed FFT analysis result.

a) Huang2 does not expressly disclose this limitation.

Petitioner alleges that “Huang2 ... discloses this element.” Pet. 35. However, Petitioner points to no disclosure of “major adjacent peaks that are about 180° apart from each other” in Huang2. *Id.* at 35–39. Petitioner could not do so because, by its own admission, Huang2 discloses a *single* peak. *Id.* at 36 (“with a ‘major peak’”). As emphasized by Petitioner’s annotation of Huang2’s Figure 1C, shown below, Huang2’s FFT result of anisotropic fibers depicts only one peak.



Pet. 36 (red annotation). Dr. Simpson agrees: “the dark line shows the FFT result ... has a *single* ‘major peak’ around about 90°.” Ex. 1003 ¶ 120 (emphasis added).

A FFT analysis result with one peak does not teach or suggest “major adjacent peaks that are about 180° apart from each other.”

Petitioner alleges that Huang2 discloses “nanofibers that are highly aligned” and “aligned in the same direction.” Pet. 35. This is inapposite; claims 1–6 do not recite “aligned” fibers. Nor do they recite a subjective interpretation of the fibers as “highly aligned.” Instead, the claims recite a specific FFT analysis result having “major adjacent peaks that are about 180° apart from each other.” Had the applicant intended to claim “highly aligned” fibers, it would have. It did not.

Accordingly, Huang2 does not satisfy this limitation.

b) Petitioner’s additional contentions likewise fail.

To cure this defect, Petitioner turns to its expert. Dr. Simpson argues that, “through its inherent mathematical properties,” a FFT analysis “produces a symmetrical plot” such that “a single peak in a 2D FFT alignment plot from 0° to 180° indicates that the plot from 0° to 360° has adjacent major peaks that are 180° apart from each other.” Pet. 9 (citing Ex. 1003 ¶¶ 46–47), 37 (“intrinsic symmetry”). Thus, Petitioner contends that reporting a FFT analysis result “beyond 180° is unnecessary”; a second major peak “would necessarily” exist between 180° and 360°, due to the alleged symmetry. Pet. 9, 28, 37.

Therefore, Petitioner contends that, “if the scale [of Huang2’s FFT analysis] were extended to 0°–360°,” then “Huang2’s FFT analysis would necessarily show a

second major peak around 270°.” *Id.* at 37. Petitioner argues that a POSITA “would know from the alignment of the fibers depicted in the image of Figure 1B and the major peak at around 90° in Figure 1C that the fibers are aligned, such that there would be a second peak about 180° apart at 270°.” *Id.* (citing Ex. 1003 ¶¶ 47, 121).

These allegations fail in numerous ways.

(1) Expert testimony cannot fill in gaps to supply missing claim limitations.

Petitioner cannot rely on expert testimony to fill gaps in Huang². *Inter partes* review is limited to review based on “patents and printed publications,” which Dr. Simpson’s testimony plainly is not. 35 U.S.C. § 311(b); *Qualcomm Inc. v. Apple Inc.*, No. 23-1208, slip op. at 17 (Fed. Cir. Apr. 23, 2025) (“Section 311(b) states that a petitioner ‘may request to cancel as unpatentable’ claims ‘only on the basis of prior art consisting of patents or printed publications.’ This means that ‘the basis’ of an IPR ground asserting unpatentability can ‘only’ include ‘prior art consisting of patents or printed publications.’”).

Furthermore, case law and guidance confirm that expert testimony cannot be used to fill gaps in Petitioner’s references. *See, e.g., Scripps Clinic & Rsch. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991) (overruled on other grounds, *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282 (Fed. Cir. 2009)) (“The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill ..., not to fill gaps in the reference.”); PTAB Consolidated

Trial Practice Guide (Nov. 2019) (“CTPG”) 36 (“[E]xpert testimony may explain ‘patents and printed publications,’ but is not a substitute for disclosure in a prior art reference itself.”).

(2) Petitioner does not meet its burden.

It is unclear if Petitioner relies on Dr. Simpson’s testimony to argue that Huang2 *inherently* teaches the claimed FFT analysis result or that this would have been obvious. Petitioner does not identify either theory with specificity. Pet. 35–39. For example, Petitioner references “inherent” mathematical properties, suggesting its argument turns on inherency. *Id.* at 9 (“inherent”), 37 (“would necessarily show”).¹⁴ But Petitioner also argues that “if the scale ... were extended,” then a major adjacent peak would exist, suggesting its argument turns on obviousness. *Id.* at 37. “[I]t is the petitioner’s burden to present a clear argument.” *Netflix, Inc. v. DivX, LLC*, 84 F.4th 1371, 1377 (Fed. Cir. 2023). Petitioner fails to do so and, regardless, Petitioner fails.

Regarding a modification to Huang2, Petitioner fails to present a reason *why* a POSITA would have been motivated to modify Huang2’s FFT analysis result, which Petitioner acknowledges is plotted to 180°, to instead plot the graph to 360°.

¹⁴ “The keystone of the inherency doctrine is inevitability.... Absent inevitability, inherency does not follow even from a very high likelihood that a prior art method will result in the claimed invention.” *In re Montgomery*, 677 F.3d 1375, 1384 (Fed. Cir. 2012).

See Pet. 37–39. Petitioner simply argues that “because of the intrinsic symmetry of an FFT, Huang2’s FFT analysis would necessarily show a second major peak at around 270° (which is 180° from the 90° peak) *if the scale were extended* to 0°–360°.” Pet. 37 (emphasis added). But this is not a motivating reason to modify Huang2. Petitioner does not even attempt to provide a rationale.

Even accepting Petitioner’s contention *arguendo*—that a POSITA would have modified Huang2’s FFT analysis result to report the graph to 360°—Petitioner fails to show that, even if so extended, “major adjacent peaks that are about 180° apart from each other” inherently would exist. The evidence Petitioner relies upon is simply insufficient.

(a) Dr. Simpson’s Testimony

Petitioner relies on Dr. Simpson to support this conclusion. Pet. 9, 12–14, 27–29, 37–39 (citing Ex. 1003 ¶¶ 46–47, 63, 65, 90, 96, 121, 125–126). However, the cited testimony is conclusory and entitled to little or no weight. 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”).

The cited paragraphs of Dr. Simpson’s declaration do not disclose sufficient underlying facts, data, or technical reasoning to support the conclusion that “the 2D FFT output image is symmetric about the horizontal axis, so a pixel summation to 360° is unnecessary.” *See* Ex. 1003 ¶ 47. Dr. Simpson simply states this conclusion

without explaining how or why it is reached.

For example, at paragraph 47, Dr. Simpson’s testimony simply circles around itself: “[T]he 2D FFT output image is symmetric about the horizontal axis, so a pixel summation to 360° is unnecessary. As a way of further explanation, the fact that the 2D FFT output image is symmetric about the horizontal axis, ensures that the peaks in the 2D FFT alignment plot repeat between 0°–180° and 180°–360°.” This statement does not provide “further explanation” of how or why the “2D FFT output image is symmetric”; it is simply a circular conclusion that improperly relies on itself for support. *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (PTAB Aug. 24, 2022) (precedential) (“[Petitioner’s expert] does not cite to any additional supporting evidence or provide any technical reasoning to support his statement.... [The] testimony is conclusory and unsupported, adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight.”); *Honeywell Int’l Inc. v. 3G Licensing, S.A.*, 124 F.4th 1345, 1354 n.6 (Fed. Cir. 2025) (“[C]onclusory expert testimony does not qualify as substantial evidence.”). The additionally cited paragraphs, Ex. 1003 ¶¶ 63, 65, 90, 121, 125–126, fare no better.

Accordingly, Dr. Simpson’s testimony should be given little or no weight. The only additional evidence cited to support the conclusion of symmetry—Dr. Simpson’s own past papers—are similarly insufficient, as detailed below.

(b) Dr. Simpson's Identified Evidence

To the extent Dr. Simpson cites evidence, but does not sufficiently discuss or explain it, that evidence is also insufficient. Indeed, to support his symmetry conclusion, Dr. Simpson cites only to his own past papers, which do not provide independent corroboration. *See, e.g.*, Ex. 1003 ¶ 47 (citing Ex. 1010; Ex. 1013.).¹⁵

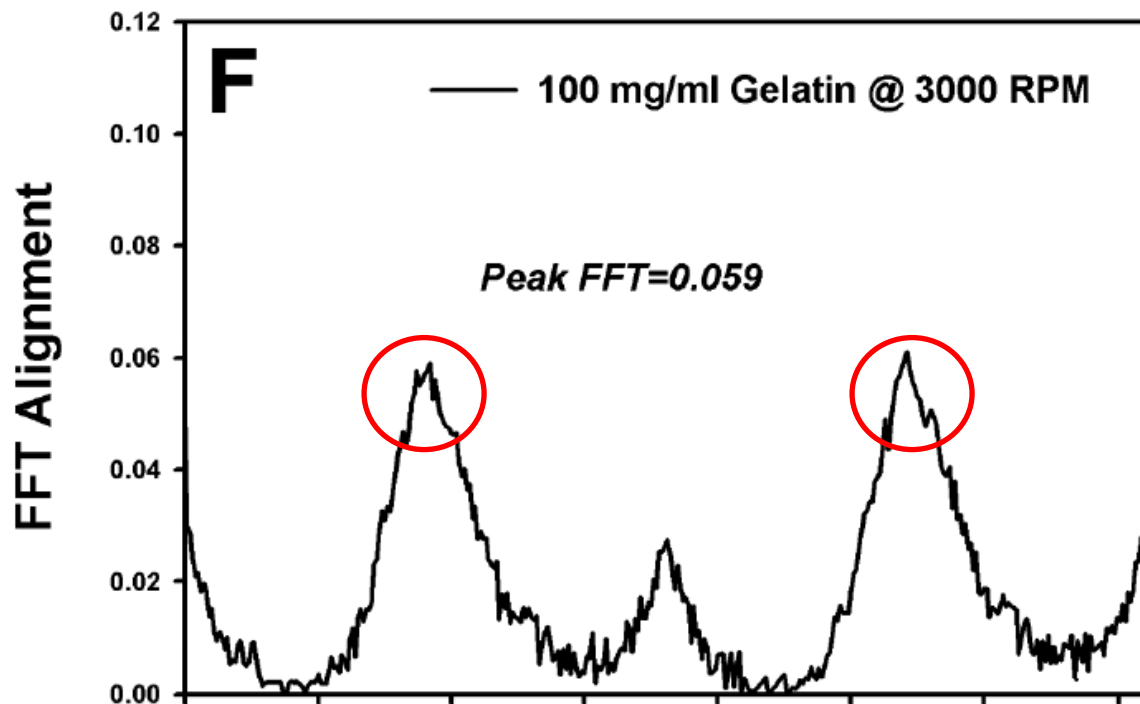
Like his declaration, these papers fail to provide sufficient underlying facts, data, or technical reasoning to support the conclusion that FFT analyses are necessarily and always symmetric about the horizontal axis. Dr. Simpson's 2008 paper, for example, states: "Typically, the data from this analysis is reported for 0 to 180°; the frequency plot is symmetric so a complete summation from 0 to 360° is not technically necessary." Ex. 1010, 609. But the discussion ends there. The paper provides no support for this statement, despite identifying independent footnote support for other statements in the same section. *See id.*

Moreover, the 2008 paper itself undermines Dr. Simpson's testimony. First, Dr. Simpson does not explain the pertinence of the term "Typically," in the sentence above. Dr. Simpson concludes that Huang2's FFT analysis result *necessarily*—not

¹⁵ Other named authors, junior to Dr. Simpson, appear on these papers. Pet. 11 ("Dr. Simpson, whose declaration is included herein, is the senior author of the Ayres paper."); Ex. 1003 ¶ 62 ("I am one of the authors...."). However, as detailed below, these papers suffer from the same lack of underlying data and technical reasoning as Dr. Simpson's declaration testimony and are equally conclusory.

typically—has major adjacent peaks that are about 180° apart from each other, due to the alleged symmetry (Pet. 37). But the use of “Typically” here casts doubt on whether major adjacent peaks are *necessarily* present. Furthermore, Dr. Simpson’s paper itself presents FFT analysis results plotted to 360° , not 180° , undermining Dr. Simpson’s testimony that plots to 180° are “typical[.]” Ex. 1010, 608 (Figures 1C/F/I plotted to 360°); *see also* Ex. 1008, 311 (Figures 4E/F plotted to 360°).

Additionally, the FFT plots in Dr. Simpson’s 2008 paper appear inconsistent with Dr. Simpson’s statement that that peaks between 0° – 180° necessarily repeat between 180° – 360° , further discrediting Dr. Simpson’s unsupported statements. Ex. 1003 ¶ 47. Figure 1F of the 2008 paper is annotated and reproduced.



Ex. 1010, 608 (annotated circles). In Figure 1F, for example, the FFT analysis result depicts two peaks, wherein the first large peak that appears near 90° varies in its shape, including its rise and fall, as compared to the second large peak appearing near 270°. For example, the top of the peak near 90° includes three ridges, while the top of the peak near 270° presents a smoother peak. *See also id.* at Figs. 1C, 1I (also depicting variations across peaks).

These peaks do *not* necessarily appear to be “repeats” of each other. *Contra* Pet. 12 (“[T]he peaks from 180° to 360° are repeats of the peaks from 0° to 180°.”); Ex. 1003 ¶ 46. Dr. Simpson declined to provide any support or explanation for his testimony regarding the extent of repetition that he contends is necessarily present. Accordingly, Dr. Simpson’s unsupported conclusion conflicts with the record and warrants little to no weight. *See Homeland Housewares, LLC v. Whirlpool Corp.*, 865 F.3d 1372, 1378 (Fed. Cir. 2017) (“[W]e must disregard the testimony of an expert that is plainly inconsistent with the record.”).

Dr. Simpson’s second cited paper fares no better. This paper also states that “the FFT is symmetric about the horizontal axis so a pixel summation to 360° is unnecessary,” but again, with no identified support. Ex. 1013, 4.

(c) Dr. Simpson’s Testing

Finally, Petitioner relies on Dr. Simpson’s own post-hoc testing to bolster its assertion that Huang2’s FFT analysis result necessarily has major adjacent peaks

that are about 180° apart from each other. Pet. 37–39 (citing Ex. 1003 ¶¶ 125–126). But this testing offends the Board’s rules, which require that Dr. Simpson provide testimony to explain “[h]ow the test was performed and the data was generated.” 37 C.F.R. § 42.65(b). Accordingly, it is entitled to little to no weight.

Rather than explain how his post-hoc testing was performed, Dr. Simpson simply states: “I conducted my own analysis of Figure 1B [of Huang2] using the FFT analysis and ImageJ software described in Huang2 and the ’227 patent. I report the data from 0° to 360°.” Ex. 1003 ¶ 125. This is the extent of explanation and is insufficient to satisfy § 42.65(b). *See Abbott Vascular, Inc. v. Flexstent*, IPR2019-00882, Paper 48 at 35 (PTAB Oct. 2, 2020) (excluding a declaration for failure to satisfy §42.65(b) where it “lacks adequate details” and “does not describe the test used[,] ... whether the test used was one known and accepted in the art,” or “how the data [the expert] collected was used to determine the values reported in his Declaration”); *Luitpold Pharms., Inc. v. Kovi et al.*, IPR2018-01640, Paper 19 at 23–24 (PTAB Mar. 6, 2019) (finding that an expert declaration that “fails to provide any specificity as to the steps taken” and “provides no independent testing data” to be insufficient evidence);.

In addition to Dr. Simpson’s failure to explain his testing protocol, the record raises independent concerns. First, Huang2 and the ’227 patent employ FFT analyses described in different papers, so it is unclear which analysis Dr. Simpson

employed when he states that he “conducted my own analysis ... using the FFT analysis and ImageJ software described in Huang2 *and* the ’227 patent.” Ex. 1003 ¶ 125 (emphasis added). Namely, the FFT analysis employed by Huang2 relies upon Dr. Simpson’s 2006 paper (Ex. 1013), *see* Ex. 1005, 1792 at 2.2, while the ’227 patent relies upon the FFT analysis discussed in Dr. Simpson’s 2008 paper (Ex. 1010), *see* Ex. 1001, 13:38–46. Petitioner does not establish that these analyses are the same.¹⁶

Second, the 2008 paper, incorporated by reference into the ’227 patent, describes various aspects of FFT analysis that are essential to accurate testing but are not acknowledged in Dr. Simpson’s post-hoc testing of Huang2’s images. For example, the 2008 paper explains that images should be “stored and analyzed as uncompressed .TIF files to preserve image integrity; the image compression used in .JPG format will degrade image integrity.” Ex. 1010, 607. Dr. Simpson does not explain how he obtained the image utilized in his testing; therefore, it is unknown to what extent image integrity degraded. Ex. 1003 ¶¶ 125–126.

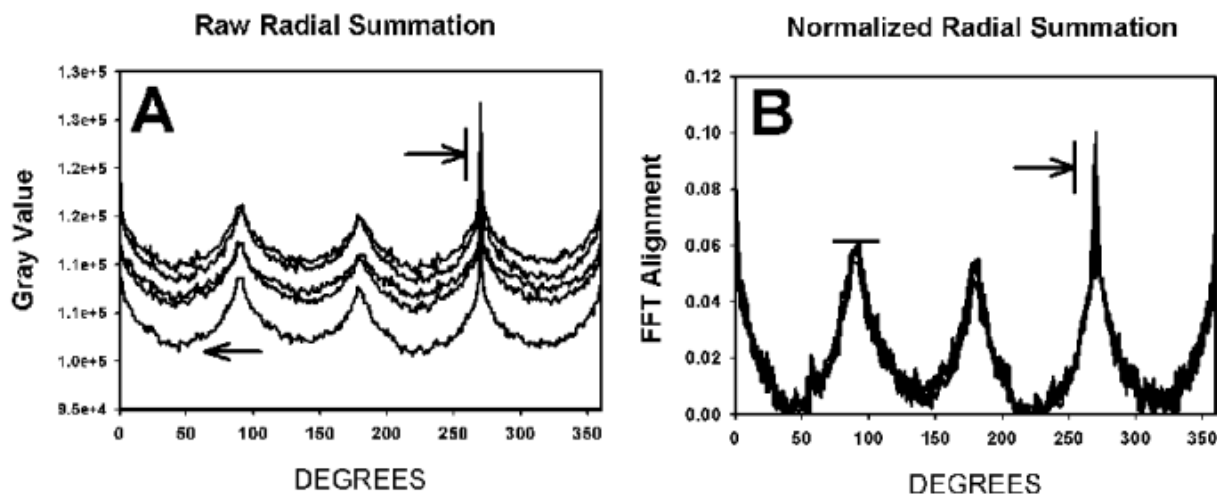
¹⁶ Despite baldly claiming that these FFT analyses are the same, Petitioner fails to establish as much. Pet. 36. Petitioner provides insufficient bases to determine that these papers disclose the same FFT process or that the same version of software was used. *Id.*; *compare* Ex. 1010, 607–609, 611–612, 615 (discussing aspects of image type, calibration, software version, illumination, variations in light intensity, optical and electronic noise, and masks that are important to FFT analysis), *with* Ex. 1013 (providing no discussion of these aspects).

The 2008 paper also explains that “[a]ngle information concerning the principle direction of fiber alignment must be calibrated to the specific version of the NIH ImageJ software and oval profile plugin used for analysis” because “[s]ome versions of ImageJ (1.36b) altered [standard] convention.... Minor corrections were incorporated into our analysis to correct for this condition, but may not be necessary for all 2D FFT programs.” Ex. 1010, 607. Again, Dr. Simpson does not explain which version of the software or plugin he used, whether or how calibration was completed, and to what extent error may have been introduced. Ex. 1003 ¶¶ 125–126.

Additionally, the 2008 paper highlights risks associated with uneven illumination: “Care should be taken at the time of image capture to optimize sample illumination; uneven illumination can complicate and introduce error into the alignment analysis.” Ex. 1010, 609. Again, Dr. Simpson does not establish whether the image presented in Huang²—a reproduction of a scanning electron microscope image obtained from a dated library publication (Pet. 25 n.3)—provides sufficient illumination for testing and to what extent error may have been introduced. Ex. 1003 ¶¶ 125–126; Ex. 1005, 1 (cover page with library sticker).

Unrecognized in Dr. Simpson’s analysis, the 2008 paper also states that “[n]ormalization ... is necessary to account for differences in sample thickness, camera performance, operator preference for contrast/brightness, and other variables

that impact sample illumination at the time of image capture.” Ex. 1010, 610. For example, in Figures 2A and 2B, reproduced below, the 2008 paper shows the extreme variation that arises when identical fibers are captured at five different light intensities (Fig. 2A) as compared to when those images are normalized (Fig. 2B).



Id. at 610–611. Dr. Simpson does not state whether he normalized images when he performed his testing, the extent or mechanism by which he might have done so, and to what extent error may have been introduced. Ex. 1003 ¶¶ 125–126.

The 2008 paper also explains that “as light intensity increases, the relative amount of optical noise present in a brightfield microscopic image also will increase. Detector noise functions in an inverse fashion. As light intensity is decreased and detector gain is increased to generate an image, electronic noise begins to be incorporated into the data set. Noise from either source (optical and/or electronic) can introduce artifacts into a data image and adversely impact the 2D FFT process.” Ex. 1010, 612. Once again, Dr. Simpson does not address whether noise impacted

his testing, which type of noise might have been introduced by the applied light intensity, or how he might have accounted for that. Ex. 1003 ¶¶ 125–126.

Finally, the 2008 paper also discusses notable artifacts in the FFT analysis that may be caused by the array of fibers in the image, as shown in Figure 3N. Ex. 1010, 614–15. “Th[e] noise effect is quite pronounced in a model scaffold containing aligned fibers that are arrayed approximately 45° with respect to the edges of the image.... The unmasked image produces a 2D FFT alignment plot with artifacts in the guise of small peaks on either side of the alignment peaks (Fig. 3N, arrows). Processing the image with a window mask removes this spurious information without altering the height of the alignment peaks (i.e., 2D FFT alignment value, Fig. 3N). Although this type of mask can be useful in many applications, it reduces the total surface area available for analysis.” Dr. Simpson’s testing depicts a mask. *See* Ex. 1003 ¶ 125, Fig. 2A (figure caption, “cropped and masked”). But Dr. Simpson does not discuss the impact of the mask’s “reduc[tion of] the total surface area available for analysis,” and to what extent that may have affected his testing.

In sum, Dr. Simpson’s testing protocol is essentially unknown. Dr. Simpson’s own 2008 paper lays bare the holes in his post-hoc testing. Lacking the required explanation, Patent Owner and the Board cannot fairly understand “[h]ow the test was performed and the data was generated.” For at least these reasons,

Dr. Simpson’s post-hoc testing of Huang2’s images is entitled to little or no weight.

c) Conclusion

Ultimately, it is Petitioner’s burden to show—in the Petition itself—why the claims it challenges are unpatentable under the legal theories Petitioner chose to present. *See Harmonic*, 815 F.3d at 1363 (“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.”); *see also Dynamic Drinkware*, 800 F.3d at 1378 , 829 F.3d 1364, 1375 (Fed. Cir. 2016) (“[A]nd that burden never shifts to the patentee.”). Petitioner fails to do so.

Petitioner fails to establish that Huang2 teaches or suggests “a result of a FFT analysis” having “major adjacent peaks that are about 180° apart from each other.” The FFT analysis result disclosed in Huang2 plainly has only a single peak. Petitioner’s argument that a POSITA could have expanded Huang2’s FFT to 360° lacks *any* identified rationale to motivate such a change. Moreover, Petitioner fails to demonstrate that, even if so modified, the FFT analysis result would necessarily include major adjacent peak that are about 180° apart from each other. Dr. Simpson’s unsupported testimony and unexplained testing protocol cannot fill these gaps in the reference on which Petitioner chose to rely.

Petitioner alone defines its grounds of unpatentability and Petitioner alone must meet its burden – *in the Petition*. A Petition’s failure to satisfy a *prima facie*

case cannot be cured through further briefing. CTPG (Nov. 2019) 73 (“Petitioner may not submit new evidence or argument in reply that it could have presented earlier, e.g. to make out a prima facie case of unpatentability.”); *Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.*, 853 F.3d 1272, 1286 (Fed. Cir. 2017) (“It is of the utmost importance that petitioners in the IPR proceedings adhere to the requirement that the initial petition identify with particularity the evidence that supports the grounds for the challenge to each claim.”).

For at least this reason, which infects all challenged claims, the Petition should be denied.

2. Neither Huang2 nor Kuo teach or suggest the claimed crosslinked collagen fibers.

Independent claim 1 also requires that the scaffold comprise “crosslinked fibers comprising collagen.” Ex. 1001, 23:31–32. Petitioner relies on Huang2, but it fails to disclose a scaffold with crosslinked fibers. Pet. 33.

Huang2 discloses that because electrospun collagen fibers experience “rapid degradation and poor mechanical properties,” “*either* crosslinking *or* combination with other materials is necessary to obtain a stable scaffold.” Ex. 1005, 1791 (emphasis added). In other words, Huang2 discloses that a choice is made to achieve stability: *either* blend collagen with another material *or* crosslink the collagen fibers. Huang2 made its choice, electing to utilize “a blend solution of collagen and polycaprolactone (PCL)” to “yield rather stable nanofibers.” *Id.* Huang2 does not

utilize a scaffold with crosslinked fibers.

Petitioner's alternate contention based on Meniel (allegedly incorporated into Kuo) also fails. Pet. 33–34 (citing Ex. 1018 ¶ 40; Ex. 1023). Petitioner relies on Meniel as disclosing that “crosslinking collagen scaffolds can address” the degradation issue. *Id.* at 34 (citing Ex. 1003 ¶ 112; Ex. 1023, 380–381, 390).

But the Petition does not present any evidence demonstrating that a POSITA would have found it obvious to crosslink Huang2's fibers, which comprise a blend of PCL and collagen, to further “improve the stability” beyond that already achieved by blending collagen with PCL. Pet. 34. Petitioner's contention of further improved stability is not supported by evidence. *Id.* Indeed, Huang2 suggests the opposite by stating that either blending or crosslinking is necessary and *not* suggesting that both steps be undertaken. Ex. 1005, 1791.

Moreover, Petitioner's reliance on Meniel is inapposite. Meniel only teaches to crosslink pure collagen and does not crosslink a PCL/collagen blend like Huang2. Ex. 1023, 380–381. Indeed, none of the evidence cited in the Petition's discussion of crosslinking teaches to crosslink a PCL/collagen blend. *See* Pet. 7 (citing Ex. 1005, 1791; Ex. 1006, 7; Ex. 1009 ¶¶ 11, 136, 137); Ex. 1003 ¶ 55 (same).

Petitioner's expert is of no help here. Dr. Simpson alleges that “a skilled artisan ... would have been motivated to improve the stability of collagen fibers by chemically crosslinking, as taught by both Huang2 and Kuo.” Ex. 1003 ¶ 114. But

even if Petitioner had relied on this testimony in its Petition (it did not), this testimony is conclusory and unsupported; Dr. Simpson provides utterly no evidence, data, or technical reasoning to support his opinion. 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *Xerox*, IPR2022-00624, Paper 9 at 15 (precedential) (“[T]he cited declaration testimony is conclusory and unsupported, adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight.”).

3. The Petition does not identify a sufficient reason to combine Huang2 and Kuo.

Petitioner fails in its reliance on Kuo to suggest that a POSITA would have used Huang2’s scaffold to repair a tendon, ligament, or nerve defect, especially where Huang2 and Kuo teach non-interchangeable structures specifically designed to repair different tissue types. Pet. 28–30.

a) Petitioner’s contention that the references are in the same field and solve the same problem is insufficient.

Petitioner bears the burden to provide articulated and supported reasoning as to *why* a POSITA would have made the proposed modification. *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (“To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The

petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.”).

Petitioner’s contention that Huang² and Kuo “are in the same field of art, and both seek to solve the same problems” is legally insufficient; it offers nothing about the specific references at issue and is silent regarding whether or why a skilled artisan would have modified one reference in view of another. Instead, at best, Petitioner alleges only that the two references existed independently in the same universe of prior art. *See, e.g., Sisvel Int’l S.A. v. Sierra Wireless, Inc.*, 82 F.4th 1355, 1364 (Fed. Cir. 2023) (“We agree with the Board that [the] first, second, and third reasons to combine were merely assertions that the references were analogous art, which, without more, is an insufficient articulation for motivation to combine”); *Securus Techs., Inc. v. Global Tel*Link Corp.*, 701 Fed. App’x 971, 977 (Fed. Cir. 2017) (unpublished) (“[A] broad characterization of [prior art references] as both falling within the same alleged field . . . without more, is not enough for [Petitioner] to meet its burden of presenting a sufficient rationale to support an obviousness conclusion.”); *Microsoft Corp. v. Enfish, LLC*, 662 Fed. App’x 981, 990 (Fed. Cir. 2016) (unpublished) (“[The] Board correctly concluded that [petitioner] did not articulate a sufficient motivation to combine.... [Petitioner] gave no reason ... except that the references were directed to the same art or same techniques.”). Thus,

Petitioner's assertion that Huang2 and Kuo are in a common field and/or solve a common problem is insufficient.

- b) Petitioner fails to demonstrate that a POSITA would have used Huang2's scaffold – specifically designed to repair skin tissue – to instead repair tendon, ligament, or nerve tissue.**

Petitioner errs in treating Huang2 and Kuo as if they are interchangeable merely because both teach scaffolds with aligned fibers. Petitioner overlooks that each scaffold is specifically designed to repair distinct types of tissue. Petitioner has not established that a POSITA would have used Huang2's skin repair scaffold to treat a tendon, ligament, or nerve defect, or would have expected success in doing so, simply because "both Huang2 and Kuo successfully created" collagen/PCL blended scaffolds and "reported obtaining aligned fibers." Pet. 30.¹⁷

- (1) Huang2 and Kuo disclose scaffolds that treat different tissue defects.**

Petitioner's proposed modification falls apart upon examination of the

¹⁷ The hindsight infecting Petitioner's grounds is laid bare by its characterization of "a tendon or ligament" as "the target tissue." Pet. 30 ("Huang2 specifically explains how aligned fibers are beneficial for cell growth, which provides further motivation to combine the two references, particularly where the target tissue is a tendon or ligament where it is important that cells grow in an aligned manner.").

A proper obviousness analysis begins with the prior art; it is improper to use the claim language itself as a "target." *See, e.g., Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570 (Fed. Cir. 1996) ("To draw on hindsight knowledge of the patented invention ... is to use the invention as a template for its own reconstruction—an illogical and inappropriate process by which to determine patentability.").

technologies disclosed by Huang2 and Kuo. Huang2 discloses scaffolds specifically designed to repair skin tissue. *See, e.g.*, Ex. 1005, Abstract (“skin wound repair”), 1791 (“skin grafts” for “closing deep skin wounds”; “skin-like tissues”; “mimic the skin ECM”), 1792 (“fabrication of functional skin grafts using electrospun nanofibers”). Huang2 does not disclose using its scaffold to repair any other tissue type, whether tendon, ligament, or nerve. *See generally* Ex. 1005.

To facilitate skin repair and wound healing, Huang2 discloses that skin fibroblast cells, which are unique to skin and absent in tendon, ligament, or nerve tissues, are “seeded on the nanofibrous matrices” and cultured for up to 7 days. *Id.* at 1792. Huang2 concludes that this approach was successful in repairing skin tissue, reporting that “NHDFs [normal human dermal fibroblasts] cultured on anisotropic PCL/collagen nanofibers showed elongated cell morphology, distinct distribution of focal adhesions, accelerated cell migration and promoted fibroblast-to-myofibroblast differentiation.” *Id.* at 1799.

By contrast, Kuo discloses scaffolds for various types of tissue repair, depending upon the cells seeded into the scaffold. *See, e.g.*, Ex. 1018, Abstract (“useful for tissue regeneration, enhancement, or tissue repair”); ¶ 58 (“[D]ifferent cell types or combinations thereof may be employed ... depending upon the intended function of the tissue engineered construct being produced.”). Kuo discloses scaffolds used to repair dozens of different tissues including ligaments, tendons,

connective tissue, nerves, nerve channels, liver, pancreas, other endothelial tissue, gastrointestinal tissue, cardiac tissue, bile ducts, other ducts, spine discs, cranial tissue, dura, kidney, bladder, spleen, cardiac muscle, skeletal muscle, breast tissues, cartilage, and bone. Ex. 1018 ¶¶ 52, 67–68. Notably, Petitioner does not allege that Kuo discloses repairing skin tissue. *See generally* Pet.

Kuo also teaches that its scaffolds are seeded with cells. Ex. 1018 ¶ 5. The cells used for seeding are chosen to facilitate growth of the desired tissue type and are “selected from the group consisting of stem cells, osteoblasts, myoblasts, neuroblasts, fibroblasts, glioblasts, germ cells, hepatocytes, chondrocytes, keratinocytes, smooth muscle cells, cardiac muscle cells, connective tissue cells, epithelial cells, endothelial cells, hormone-secreting cells, neurons, tenocytes, skeletal myocytes, and skeletal myoblasts.” *Id.* ¶¶ 16, 58.

Petitioner paints with too broad a brush in suggesting that Huang² and Kuo are interchangeable merely because they both disclose aligned fibers. The types of cells incorporated into each scaffold differ, which dictates the precise type of tissue repair that will be achieved. Ex. 1018 ¶ 58 (“[D]ifferent cell types or combinations thereof may be employed ... depending upon the intended function of the tissue engineered construct being produced.”).

(2) Huang2's scaffold is only seeded with cells that target repair of skin, and is not seeded with cells that target tendons, ligaments, or nerves.

At bottom, Petitioner's contentions amount to an argument that it would have been obvious to use Huang2's skin repair scaffold to instead repair, e.g., tendons, as taught by Kuo, because both references disclose scaffolds with aligned fibers, and aligned fibers mimic the native structure of tendons. Pet. 30 (also addressing ligaments and nerves, with similar analysis). But this rationale overlooks that Huang2's scaffold is seeded with skin cells to support skin tissue growth; it is not seeded with cells that support tendon repair (or ligament or nerve repair). *See generally* Ex. 1005. Petitioner recognizes as much: "Huang2 further discloses a 'wound healing assay' wherein nanofibrous matrices are *seeded with fibroblasts for wound treatment*." Pet. 32 (emphasis added).

Neither Petitioner nor its expert reckon with Huang2's seeding much less explain how the skin cells embedded in Huang2's scaffold would function to repair, e.g., tendon tissue. Pet. 30; Ex. 1003 ¶¶ 94–102. To the contrary, Petitioner's evidence shows that when tendon repair is intended, a scaffold is seeded with *tendon* cells (tenocytes) or with stem/progenitor cells that differentiate into other tissue types. Ex. 1018 ¶¶ 16 (tenocytes), 112 (stem/progenitor cells); *see also* Ex. 2003, 3 (Dorland's Illustrated Medical Dictionary defining "progenitor" as "1. A parent or ancestor. 2. Stem cell."); Ex. 2004, 3 (Dorland's Illustrated Medical Dictionary

defining “stem c[ell]” as “1. Any precursor cell. 2. A blood cell progenitor or mother cell representing a slightly later stage than the blast cell; It has the capacity for both replication and differentiation ...”).

As such, Petitioner fails to demonstrate that a POSITA would have been motivated to use Huang2’s skin repair scaffold, which is seeded with normal human dermal fibroblast skin cells, to repair a different type of tissue, e.g., tendon, ligament, or nerve. The record lacks any evidence on which to conclude that such use would have been successful, for example, in the absence of seeded cells specific to those particular tissues. Nor does Petitioner propose further modifying Huang2 to eliminate its fibroblast seeding and replace it with seeding of alternate cell types, e.g., tenocytes, for tendon tissue repair. Pet. 28–30.¹⁸

¹⁸ In an unsupported and conclusory statement, Dr. Simpson states that “a POSA would have been able to make and use a scaffold comprising Huang2’s aligned fibers and seeded with various cell types using well-known established methods described in both Huang2 and Kuo to achieve predictable results with a reasonable expectation of success.” Ex. 1003 ¶ 102. This statement, however, must be disregarded as it is both unsupported and presents an argument not made in the Petition itself. Petitioner must present its arguments in the Petition and cannot incorporate arguments by reference. 37 C.F.R. § 42.6(a)(3). Additionally, Dr. Simpson must support this bald conclusion, *id.* § 42.65(a), but did not.

(3) Kuo’s scaffold used for tendon and ligament repair involves a unique rolled structure that is not present in Huang2.

Kuo’s disclosure highlights additional deficiencies in Petitioner’s contentions.

Pet. 29–30 (citing Ex. 1018 ¶ 112). To repair tendon or ligament tissue, Kuo discloses that “[a]ligned nanofiber scaffolds were seeded with progenitor cells and subsequently rolled with the leading edge parallel to the axis of alignment.” Ex. 1018 ¶ 112. Kuo explains that this rolled structure “locally mimicked the native microstructure of tendon/ligament ..., globally mimicked a fascicle or bundle in tendon/ligament tissue, and resulted in cell seeding throughout the construct.” *Id.* Kuo’s success in mimicking native tissue turns in part on this three-dimensional rolled design, which presents advantages over non-rolled scaffolds like Huang2’s. *See also id.* (“This design avoids poor cell seeding ... that is a major limitation of aligned scaffolds due to their low porosity as a result of closely packed aligned fibers.”); *id.* ¶ 118 (“Rolled scaffolds supported cell adhesion and distribution throughout the three-dimensional rolled structure.”).

Petitioner does not allege that Huang2 discloses a rolled scaffold, nor does Petitioner propose modifying Huang2 to present such a structure. Neither Petitioner nor its expert present any evidence or technical reasoning to suggest that the tendon repair achieved by Kuo would have been obvious, or would have been expected to

succeed, when used with Huang2's scaffold, which lacks the unique rolled design to which Kuo attributes success.

4. Conclusion

Petitioner's asserted ground of unpatentability over Huang2 and Kuo fails. The combination of Huang2 and Kuo fail to teach or suggest the claimed FFT analysis result *and* the claimed crosslinked collagen fibers. Moreover, Petitioner fails to present an articulated reasoning with rational underpinning as to *why* a POSITA would have modified Huang2 in view of Kuo, as proposed, with a reasonable expectation of success. Accordingly, the Petition should be denied.

C. Ground 2: Petitioner Fails To Show Obviousness of Claims 1–6 over Lee Alone, or with Kuo

Petitioner's allegations based on Lee and Kuo suffer many of the same deficiencies detailed above regarding Ground 1, only amplified, because Lee does not utilize FFT *at all*. Petitioner fails to meet its burden because (1) absent any disclosure of FFT, Lee does not (and cannot) teach or suggest "a result of a FFT analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other" and (2) a POSITA would not have been motivated to modify the references.

1. Lee does not teach or suggest the claimed FFT analysis result.

a) Lee does not expressly disclose this limitation.

Petitioner contends that “Lee by itself also discloses this element.” Pet. 47. However, Lee does not disclose FFT *at all*, much less the claimed FFT analysis result. *See generally* Ex. 1011.

Petitioner alleges that Lee “investigated the impact of alignment and the orientation” of the scaffold’s fibers without FFT, including by (1) scanning electron microscopy (“SEM”) examination, (2) ImageTool 3.0 freeware analysis, and (3) tensile testing, which demonstrated that Lee’s scaffold includes “highly aligned fibers.” Pet. 47–49 (SEM and ImageTool), 51 (tensile testing). But “investigat[ing] the impact of alignment and the [fiber] orientation” is not the claimed result of a FFT analysis. And, as discussed above, the claims do not recite “aligned fibers” or a subjective interpretation of the fibers as “highly aligned.” Instead, the claims recite a specific FFT analysis result having “major adjacent peaks that are about 180° apart from each other.” Pet. 47.

Lee’s silence regarding FFT is dispositive. Lee cannot expressly disclose the claimed FFT analysis result when FFT is not employed.

b) Petitioner’s alternative contentions likewise fail.

Petitioner alternatively contends that this limitation would have been obvious. Petitioner alleges that a POSITA “would know that the degree of alignment could also be determined using ImageJ software.” Pet. 50. Petitioner contends that “if a

[POSITA] wanted to perform an FFT analysis on the SEM image in Lee, a [POSITA] could do so using the ImageJ software, and would know how to perform the straightforward analysis.... This would show the fibers were oriented on the scaffold in Lee in an aligned manner.” *Id.* at 50. Petitioner contends that a POSITA “would have been motivated to confirm the alignment of Lee’s fibers with a well-known established tool.” *Id.* at 51. Petitioner also contends that the POSITA would have expected success, as demonstrated by Dr. Simpson’s testing of Lee’s images. *Id.* at 50–51.

(1) Petitioner does not demonstrate a sufficient rationale to modify Lee to perform FFT analysis.

Petitioner fails to satisfy its burden to demonstrate a motivation to modify Lee. First, Petitioner applies the wrong standard in asserting that “*if a [POSITA] wanted to perform an FFT analysis on the SEM image in Lee, a [POSITA] could do so using the ImageJ software.*” Pet. 50. It is Petitioner’s burden to provide a sufficiently articulated reasoning with rational underpinning to explain why the POSITA would have “wanted to perform an FFT analysis”; it is insufficient to merely to allege that the modification *could* be done *if* a POSITA wanted to. Controlling case law is clear that “could have” is not the test; a credible reason to modify must be shown. *Belden, Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (“Obviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of

prior art to arrive at the claimed invention.”); *Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 888 (Fed. Cir. 2024) (“It does not suffice to simply be known. A reason for combining must exist.”).

Moreover, Petitioner acknowledges that Lee already confirms fiber alignment through three different mechanisms *other than* FFT analysis: (1) scanning electron microscopy (SEM) examination, (2) ImageTool 3.0 freeware analysis, and (3) tensile testing. Pet. 48–51. Petitioner fails to explain why a POSITA would have been motivated to *further* confirm alignment by a fourth mechanism, given that alignment has already been confirmed in three different ways. Pet. 50–51; *In re Magnum Oil Tools*, 829 F.3d at 1380 (“[A] petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.”).

For example, Petitioner does not show that a fourth confirmation mechanism based on FFT would have been needed, expected, or typical in the art. Pet. 50–51. Nor does Petitioner identify any deficiency in the first (SEM examination), second (ImageTool 3.0 analysis), or third mechanisms (tensile testing) Lee already used to confirm alignment. *Id.* Petitioner also does not contend that FFT analysis would have imparted some additional or unique benefit over the three mechanisms Lee already employed. *Id.* And while Petitioner alleges that FFT was a “well-known established tool,” the fact that Lee already employed three other confirmation

mechanisms suggests that they were “well-known established tool[s]” as well. Pet. 51; *see, e.g., Edwards Lifesciences Corp. v. Aortic Innovations LLC*, IPR2023-01232, Paper 10 at 36–37 (PTAB Feb. 7, 2024) (finding the purported motivation to be “inchoate” and “unpersuasive” because the “benefits” of the combination “are already conferred”); *see also UiPath, Inc. v. Rule 14 LLC*, IPR2024-01304, Paper 8 at 26–27 (PTAB Mar. 14, 2025) (finding no motivation to combine where the primary reference “already includes the option for the user to manually select a data source” and petitioner and its expert offered only conclusory argument in support of the combination). Dr. Simpson’s near verbatim testimony fares no better. Ex. 1003 ¶¶ 181–187.

Petitioner was required to identify and support any purported motivation to modify Lee in the Petition; this failure in its *prima facie* case cannot be cured post-institution. “Because of the expedited nature of IPR proceedings, it is of the utmost importance that petitioners in the IPR proceedings adhere to the requirement that the initial petition identify with particularity the evidence that supports the grounds for the challenge to each claim.” *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1330 (Fed. Cir. 2019); *see also AMP Plus, Inc. v. DMF, Inc.*, 2025 U.S. App. LEXIS 6374 (Fed. Cir. 2025) (“[T]he law of obviousness does not require the court, or the Board, to develop arguments for a limitation that the petition simply did not make.”).

Finally, Petitioner relies upon Dr. Simpson’s post-hoc testing to support its

contention that a POSITA would have expected success in applying FFT analysis to Lee. Pet. 50–51; Ex. 1003 ¶ 187 (“[A POSITA] would have more than a reasonable expectation of success of successfully running an FFT on Lee’s SEM images, as demonstrated by my above success in running an FFT analysis.”). However, the obviousness inquiry concerns the time of invention, not the time an expert declaration is prepared. Even if Dr. Simpson’s post-hoc testing protocol was explained (it was not; 37 C.F.R. § 42.65(b)) and even if this testing was not deficient (it was, *see supra* V.B.1.b.2.c), this testing is insufficient to show that a POSITA *at the time* of invention would have expected success. *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 974 (Fed. Cir. 2014) (“Obviousness, and expectation of success, are evaluated from the perspective of a person having ordinary skill in the art at the time of invention.”).

As such, Petitioner fails to demonstrate that a POSITA would have been motivated to modify Lee. Petitioner’s obviousness ground fails on that basis alone.

(2) Even if a POSITA would have performed FFT analysis, Petitioner’s evidence is insufficient to satisfy the FFT analysis result limitation.

Even if the Board were to accept *arguendo* that a POSITA would have been motivated to perform a FFT analysis on Lee’s images, Petitioner fails to show that a FFT analysis result necessarily would demonstrate major adjacent peaks that are about 180° apart from each other. The evidence Petitioner relies upon is simply

insufficient.

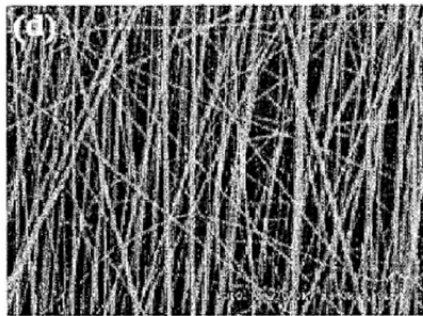
As above, *see supra* Section V.B.1.b. (incorporated herein), Petitioner relies on Dr. Simpson to support this conclusion. Pet. 50–51 (citing Ex. 1003 ¶¶ 181–187). This approach, however, contravenes the statutory requirement that asserted grounds be premised on “patents or printed publications.” 35 U.S.C. § 311(b). It is improper for Petitioner to rely on Dr. Simpson’s testimony to bridge that gap in the reference. *See Scripps*, 927 F.2d at 1576.

Moreover, Dr. Simpson’s testimony regarding the result of a FFT analysis—if even performed on Lee’s images—turns entirely on Dr. Simpson’s post-hoc testing. Pet. 50–51 (citing Ex. 1003 ¶¶ 181–187). But this testing is entitled to little or no weight because Dr. Simpson again provides insufficient explanation of his testing protocol, stating only that “I conducted my own analysis on Lee’s Figure 1D using the FFT analysis described in the ’227 patent. I report the data from 0° to 360°.” Ex. 1003 ¶ 183. This is the only cited portion of Dr. Simpson’s declaration explaining “[h]ow the test was performed and the data was generated” and is insufficient.¹⁹ 37 C.F.R. § 42.65(b); *Luitpold Pharms.*, IPR2018-01640, Paper 19 at 23 (PTAB Mar. 6, 2019) (finding that an expert declaration that “fails to provide any

¹⁹ Paragraph 182 of the declaration generally discusses how FFT analysis works. Ex. 1003 ¶ 182. This paragraph it does not explain how Dr. Simpson’s own testing of Lee’s image was performed.

specificity as to the steps taken” and “provides no independent testing data” is insufficient evidence); *see also Abbott*, IPR2019-00882, Paper 48 at 35 (PTAB Oct. 2, 2020).

Dr. Simpson purports to have analyzed Figure 1D from Lee’s provisional application, reproduced below. Ex. 1003 ¶ 179.



Immediately apparent from visual inspection of this image is its poor image quality. The record establishes the importance of image quality in the FFT analysis, casting doubt on the veracity of Dr. Simpson’s testing or its purported results. *See, e.g.*, Ex. 1010, 605 (“If an objective with inadequate resolving power is used to capture data sets, individual fibers are not detected and the resulting image is composed largely of optical noise. In general, this type of optical image/data set is unsuitable for analysis.”). Dr. Simpson does not reckon with this image quality or the extent of “optical noise” it depicts. *Id.*

Additionally, Dr. Simpson purports to have performed the FFT analysis described in the ’227 patent, which incorporates Dr. Simpson’s 2008 paper by reference. As discussed above, *see supra* V.B.1.b.2 and incorporated herein by

reference, the 2008 paper describes various aspects of the FFT analysis that are essential for accuracy but are not acknowledged by Dr. Simpson's post-hoc testing. Specifically, Dr. Simpson does not establish that he accounted for:

- image compression and storage type (*see* Ex. 1010, 607 (discussing the importance of using uncompressed .TIF files “to preserve image integrity”));
- necessary calibration for certain versions of ImageJ software and oval profile plugin (*see id.* (explaining that “[s]ome versions of ImageJ (1.36b) altered [standard] convention,” necessitating “[m]inor corrections ... [which] may not be necessary for all 2D FFT programs”));
- uneven illumination (*see id.* at 609 (explaining that “[c]are should be taken ... to optimize sample illumination; uneven illumination can complicate and introduce error into the alignment analysis”));
- variations in light intensity (*see id.* at 610–612 (explaining that “[n]ormalization ... is necessary to account for differences in sample thickness, camera performance, operator preference for contrast/brightness, and other variables that impact sample illumination at the time of image capture”));
- optical and electronic noise (*see id.* at 612 (explaining that “[n]oise from either source (optical and/or electronic) can introduce artifacts into a data image and adversely impact the 2D FFT process”)); or

- fiber array and any applied mask (*see id.* at 615 (explaining that noise may be introduced with “fibers that are arrayed approximately 45° with respect to the edges of the image” such that “[t]he unmasked image produces a 2D FFT alignment plot with artifacts in the guise of small peaks on either side of the alignment peaks,” but also recognizing that application of a mask “reduces the total surface area available for analysis”).

Dr. Simpson does not explain how any aspect of his testing was performed, violating 37 C.F.R. § 42.65(b), and certainly does not establish that his testing conditions were sufficient to ensure reliable results.

For at least these reasons, Dr. Simpson’s post-hoc testing of Lee’s image is entitled to little or no weight.

c) Conclusion

Lee does not employ FFT at all, let alone the FFT analysis result as claimed. Moreover, Petitioner fails to demonstrate that a POSITA would have found it obvious to perform a FFT analysis in Lee, especially where alignment already has been confirmed in multiple ways. Finally, even if a POSITA had done so, Petitioner’s sole argument to demonstrate the presence of major adjacent peaks—Dr. Simpson’s post-hoc testing—is insufficient.

2. Lee alone does not disclose or render obvious use of Lee’s scaffold to repair a tendon, ligament, or nerve defect

Claim 1 further recites, “applying the scaffold to the tissue defect to repair a

tendon, a ligament or a nerve defect.” Ex. 1001, 23:36–37. Petitioner acknowledges that “Lee does not expressly disclose using his scaffolds to repair a tendon, ligament, or nerve defect,” but asserts that this would have been obvious based on Lee alone, “given the similarities between the tissue” types. Pet. 51–52. Not so.

Lee discloses scaffolds specifically designed to repair muscle tissue. *See, e.g.*, Ex. 1011, Abstract (disclosing “methods of treating a subject in need of skeletal muscle reconstruction”), ¶ 2 (“The present invention ... involves the engineering of muscle tissues.”). Lee does not disclose repairing any other tissue type, whether tendon, ligament, or nerve. *See generally* Ex. 1011.

To facilitate muscle tissue repair, Lee explains that “it is preferable to mimic native skeletal muscle construction, with its highly oriented fibers of fused mononucleated muscle cells. The ability to efficiently organize muscle cells to form aligned myotubes in vitro would greatly benefit efforts in skeletal muscle tissue engineering.” *Id.* ¶ 4. Thus, Lee discloses a muscle tissue repair scaffold with “aligned myotubes,” cells unique to muscle and absent in tendon, ligament, or nerve tissues. *See, e.g., id.* ¶¶ 5 (“Provided herein are muscle implants including: a biodegradable scaffold ... and mammalian myotubes in said scaffold.”), 31 (“Myotubes are elongated, multinucleated cells, normally formed by the fusion of myoblasts.”) To that end, Lee discloses that human skeletal muscle cells (hSkMCs) were seeded on Lee’s scaffold. *Id.* ¶¶ 72–73; *see also id.* ¶¶ 60. After being cultured

on the scaffold, “[t]he cells fused and formed myotubes.” *Id.* ¶ 82. Clearly, Lee’s disclosure is specifically directed to muscle tissue repair. As such, Petitioner’s contention that it would have been obvious to use Lee’s scaffold to repair other tissues is inconsistent with the reference itself.

The only evidence put forth to support this contention of obviousness over Lee alone is Dr. Simpson’s testimony that “it would have been well-understood by a POSA that Lee’s scaffold ... could also have been used to treat a tendon or ligament injury given the similarities between the tissue, thus rendering this claim element obvious. Indeed, Kuo even uses the same scaffold for muscles, tendon, nerve, and ligament.” Ex. 1003 ¶ 188 (citing Ex. 1018 ¶ 5); Pet. 51–52 (citing Ex. 1003 § VI.B.1.d (*id.* ¶¶ 188–199)). But this testimony is fatally flawed.

First, expert testimony “cannot take the place of a disclosure in a prior art reference, when that disclosure is required as part of the unpatentability analysis.... [I]n an obviousness analysis, conclusory assertions from a third party about general knowledge in the art cannot, without supporting evidence of record, supply a limitation that is not evidently and indisputably within the common knowledge of those skilled in the art.” CTPG 36 (citing *K/S Himpp v. Hear-Wear Techs., LLC*, 751 F.3d 1362, 1365 (Fed. Cir. 2014)).

Second, Dr. Simpson’s testimony is conclusory and unsupported. Indeed, the sole piece of evidence cited by Dr. Simpson fails to support his own conclusion.

Kuo states: “When seeded with cells and subsequently rolled into cylindrical form, these constructs can be used to form structures e.g., similar to fascicles of the muscle, tendon, nerve, or ligament.” Ex. 1018 ¶ 5. But this does not indicate that “the same scaffold” is used to repair each of muscle, tendon, nerve, or ligament, as Dr. Simpson asserts. Ex. 1003 ¶ 188. To the contrary, Kuo explains that scaffolds are seeded with *different cell types appropriate to the type of tissue to be repaired*, e.g., scaffolds may be seeded with “skeletal myocytes, and skeletal myoblasts” to repair muscle tissue; with “tenocytes” to repair tendon tissue; or with “neurons” to repair nerve tissue. Ex. 1018 ¶ 58 (“A number of different cell types or combinations thereof may be employed ... depending upon the intended function of the tissue engineered construct being produced.”), 16 (“[T]he cell is selected from the group consisting of ... neurons, tenocytes, skeletal myocytes, and skeletal myoblasts.”).

Indeed, neither Petitioner nor its expert reckon with the seeding incorporated in Lee’s scaffold, much less explain how Lee’s scaffold seeded with muscle cells would have functioned to repair, e.g., tendon tissue. Pet. 51–52; Ex. 1003 ¶¶ 188–198. To the contrary, the record evidence shows that when tendon repair is intended, a scaffold is seeded with *tendon* cells (tenocytes) or stem/progenitor cells that differentiate into other cellular types. Ex. 1018 ¶¶ 16, 112; Ex. 2003, 3; Ex. 2004, 3. Accordingly, Dr. Simpson’s testimony lacks sufficient support and should be afforded little to no weight. 37 C.F.R. 42.65(a).

Petitioner fails to demonstrate that a POSITA would have been motivated to use Lee’s muscle repair scaffold, seeded with human skeletal muscle cells, to repair a different type of tissue, e.g., tendon, ligament, or nerve. Petitioner fails to provide any evidence to suggest this would have been successful, let alone in the absence of seeded cells specific to those tissue types. Pet. 51–52. Nor does Petitioner propose further modifying Lee to eliminate its muscle cell seeding and replace it with cells of alternate types, e.g., tenocytes, for use in repairing that type of tissue. *Id.* Petitioner was required to present any such argument or evidence in the Petition.

Finally, Dr. Simpson’s focus on whether a POSITA “could also have” used Lee’s structure to treat tendon or ligament injury is beside the point. Ex. 1003 ¶ 188 (“Lee’s scaffold ... could also have been used to treat a tendon or ligament injury.”). The proper inquiry is not whether a POSITA *could* have done so; the pertinent question is whether a POSITA *would* have been motivated to do so with a reasonable expectation of success. Dr. Simpson fails to address the legally operative question. *See Belden*, 805 F.3d at 1073 (“Obviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention.”).

3. The Petition does not identify a sufficient reason to combine Lee and Kuo.

Petitioner fails in its alternate reliance on Kuo to suggest that a POSITA would have used Lee’s scaffold to repair a tendon, ligament, or nerve defect, especially

where Lee and Kuo teach non-interchangeable structures specifically designed to repair different tissue types. Pet. 52–54.

a) Petitioner’s contention that the references are in the same field and solve the same problem is insufficient.

As discussed with respect to Ground 1, Petitioner is misguided in relying upon an allegedly common field of art or problem to be solved. This does not constitute an articulated reasoning with rational underpinning as to *why* a POSITA would have modified Lee in view of Kuo as proposed. *See supra* Section V.B.3.a (incorporated herein).

b) Petitioner fails to demonstrate that a POSITA would have used Lee’s scaffold – specifically designed to repair muscle tissue – to instead repair tendon, ligament, or nerve tissue.

Petitioner errs in treating Lee and Kuo as if they are interchangeable merely because both teach scaffolds with aligned fibers. Petitioner overlooks that each scaffold is specifically designed to repair distinct types of tissue. Petitioner has not established that a POSITA would have used Lee’s muscle repair scaffold to treat a tendon, ligament, or nerve defect, or would have expected success in doing so, simply because “both Lee and Kuo successfully created” collagen/PCL blended scaffolds and “reported obtaining aligned fibers.” Pet. 53–54.

(1) Lee and Kuo disclose scaffolds that treat different tissue defects.

Lee’s scaffold, specifically designed for repair of muscle tissue, is described

above in Section V.C.2. Lee discloses that human skeletal muscle cells (hSkMCs) were seeded onto the scaffolds to facilitate myotube formation and muscle repair. Ex. 1011 ¶¶ 72–73.

Kuo is described above in Section V.B.3.b. In contrast to Lee, Kuo’s scaffold may be used for repair of various tissue types depending upon the cells seeded into the scaffold. Ex. 1018 ¶ 58 (“A number of different cell types or combinations thereof may be employed ... depending upon the intended function of the tissue engineered construct being produced.”). For example, Kuo’s scaffolds may be seeded with “tenocytes” to repair tendon tissue. *Id.* ¶ 16 (“[T]he cell is selected from the group consisting of ... tenocytes.”).

As above, Petitioner paints with too broad a brush in suggesting that Lee and Kuo are interchangeable merely because they both disclose aligned fibers. To the contrary, the scaffolds of Lee and Kuo differ in the types of cells incorporated into each scaffold, which dictates the precise type of tissue repair that will be achieved.

(2) Lee’s scaffold is only seeded with cells that target repair of muscles, and is not seeded with cells that target tendons, ligaments, or nerves.

Like its contentions regarding Ground 1, Petitioner alleges that it would have been obvious to use Lee’s muscle repair scaffold to instead repair, e.g., tendons, as taught by Kuo, because both references disclose scaffolds with aligned fibers, and aligned fibers mimic the native structure of tendons. Pet. 52–54 (also addressing

ligaments and nerves, with similar analysis). But this rationale suffers the same defects as in Ground 1. It overlooks that Lee's aligned scaffold is seeded with muscle cells to support muscle tissue growth; it is not seeded with cells that support tendon repair (or ligament or nerve repair). *See generally* Ex. 1011.

As discussed above in Section V.C.2, neither Petitioner nor its expert reckon with Lee's seeding, much less explain how the muscle cells embedded in Lee's scaffold would function to repair, e.g., tendon tissue. Pet. 52–54; Ex. 1003 ¶¶ 188–198. To the contrary, Petitioner's evidence shows that when tendon repair is intended, a scaffold is seeded with *tendon* cells (tenocytes) or stem/progenitor cells that differentiate into other cellular types. Ex. 1018 ¶¶ 16, 112; Ex. 2003, 3; Ex. 2004, 3.

As such, Petitioner fails to demonstrate that a skilled artisan would have been motivated to use Lee's muscle repair scaffold, which is seeded with human skeletal muscle cells, to repair a different type of tissue, e.g., tendon, ligament, or nerve. The record lacks any evidence on which to conclude that such use would have been successful, for example, in the absence of seeded cells specific to those particular tissues. Nor does Petitioner propose further modifying Lee to eliminate its muscle cell seeding and replace it with seeding of alternate cell types, e.g., tenocytes, for tendon tissue repair. Pet. 52–54. Again, Petitioner was required to present any such argument or evidence in the Petition.

(3) Kuo's scaffold used for tendon and ligament repair involves a unique rolled structure that is not present in Lee.

As described above in Section V.B.3.b.3, Kuo's scaffold is prepared in a three-dimensional rolled design, which presents advantages over aligned non-rolled scaffolds like Lee's. Ex. 1018 ¶¶ 112, 118. As above, Petitioner does not allege that Lee discloses a rolled scaffold, nor does Petitioner propose modifying Lee to present such a structure. Neither Petitioner nor its expert present any evidence or technical reasoning to suggest that the tendon or ligament repair achieved by Kuo would have been obvious, or would have succeeded, when used with Lee's scaffold which lacks the unique rolled design disclosed by Kuo.

4. Conclusion

Petitioner's cited prior art fails to satisfy the claimed FFT analysis result required in independent claim 1. Moreover, Petitioner fails to present an articulated reasoning with rational underpinning as to *why* a POSITA would have modified Lee in view of Kuo, as proposed, with a reasonable expectation of success. Accordingly, Petitioner's asserted ground of unpatentability over Lee and Kuo fails.

D. Ground 3: Petitioner Fails to Show Anticipation of Claims 7–8 by Huang2

Like claim 1, independent claim 7 also recites that “a result of a FFT analysis of the fibers demonstrates that the fibers have major adjacent peaks that are about 180° apart from each other.” Ex. 1001, 24:7–9. Petitioner alleges that Huang2

discloses this limitation for the same reasons discussed regarding Ground 1. Pet. 60–61.

For the reasons discussed above, which apply equally here, Petitioner’s contentions fail. *See supra* § V. B.1. Huang2 fails to disclose, either expressly or inherently, a FFT analysis result with “major adjacent peaks that are about 180° apart from each other.” To the contrary – Huang2 discloses only a single peak. Pet. 60; Ex. 1005, Fig. 1C. And, contrary to its suggestion, Petitioner fails to establish that a second adjacent peak necessarily would have been present. *See supra* § V.B.1.

VI. CONCLUSION

For the reasons discussed above, Petitioner has failed to meet its burden under 35 U.S.C. § 314(a). Patent Owner respectfully requests that the Board deny institution of *inter partes* review.

Dated: May 6, 2025

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Certification under 37 C.F.R. § 42.24(d)

I hereby certify that this preliminary response, excluding its table of contents, table of authorities, certification under 37 C.F.R. § 42.24(d), certificate of service, and appendix of exhibits has 13,249 words as counted by Microsoft Word, the word-processing system used to prepare this preliminary response.

Dated: May 6, 2025

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Certification of Service

Pursuant to 37 C.F.R. § 42.6, the undersigned certifies that on May 6, 2025, a copy of the foregoing document and attached exhibits were served by electronic mail upon the following counsel of record for Petitioner:

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