

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.

IPR2025-00248
Patent 10,137,223 B2

Before SHERIDEN K. SNEDDEN, CHRISTOPHER G. PAULRAJ, and
CHRISTOPHER C. KENNEDY, *Administrative Patent Judges*.

PAULRAJ, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314, 37 C.F.R. § 42.4

I. INTRODUCTION

A. *Background and Summary*

Embody, Inc. and Zimmer Biomet Holdings, Inc. (collectively, “Petitioner”) filed a Petition requesting *inter partes* review of claims 1–12 of U.S. Patent Number 10,137,223 B2 (Ex. 1001, “the ’223 patent”). Paper 2 (“Petition” or “Pet.”). LifeNet Health (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 9 (“Prelim. Resp.”).

We have the authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314; 37 C.F.R. §42.4(a). We may not institute an *inter partes* review “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a).

In this decision, we address the merits of the issues raised by the parties regarding claims 1–12 of the ’223 patent. For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Because Petitioner has demonstrated a reasonable likelihood that at least one challenged claim of the ’223 patent is unpatentable, we institute an *inter partes* review of all challenged claims based on the grounds set forth in the Petition.

B. *Real Parties in Interest*

Petitioner identifies Embody, Inc. as the real parties-in-interest (“RPI”). Pet. 3. Petitioner further identifies Zimmer Biomet Holdings, Inc. (“ZBH”) as a second RPI “[o]ut o[f] an abundance of caution.” *Id.* Patent Owner identifies only itself as the RPI. Paper 3, 1. There is no dispute over the RPIs in this proceeding.

C. Related Matters

The parties identify LifeNet Health v. Zimmer Biomet Holdings, Inc., Case No. 2:23-cv-00479 (E.D. Va.) as a related matter. Pet. 3; Paper 3, 1. We also note Petitioner filed a petition for *inter partes* review for a related patent, U.S. Patent 11,318,227 in IPR2025-00249. We issue our institution decision in that proceeding concurrently with this decision.

D. The '223 Patent (Ex. 1001)

1. Specification

The '223 patent is titled “Aligned Fiber and Method of Use.” Ex. 1001, code (54). The '223 patent issued from Appl. No. 14/776,106, which was filed as a PCT application on March 13, 2014. *Id.* at codes (21), (80). The '223 patent claims priority to Provisional Appl. No. 61/785,031, filed on March 14, 2013. *Id.* at code (60).

The '223 patent discloses a scaffold comprising an aligned fiber used for tissue engineering. *Id.* at 1:10–23. It describes the use of an electrospinning apparatus to create fibers as small as one nanometer that are aligned in one principal direction, rather than being randomly oriented. *Id.* at 1:65–12:67. This electrospinning apparatus includes (i) two spinnerets with electrified tips having opposite charges and (ii) a collector with at least two grounded rods and a platform connecting the rods. *Id.* at 2:12–16. The electrified spinneret is used to extrude a polymer solution to form fibers. *Id.* at 2:62–64. As a result of the electrospinning, “the fibers align on the rod (e.g. by spinning around the rods or jumping to one rod to another) in a perpendicular angle to the rods.” *Id.* at 4:46–48. The fibers may be aligned in an angle ranging from about 90° to about 155° or less. *Id.* at 4:48–60.

The '223 patent further describes the use of fast Fourier transform (FFT) analysis to measure the degree of alignment of the electrospun fibers. *Id.* at 13:3–26. Specifically, the patent indicates that the FFT analysis may be performed using the methods described in an article titled “*Measuring fiber alignment in electrospun scaffolds: a user’s guide to the 2D fast Fourier transform approach*” by Ayres et al., which is incorporated by reference into the '223 patent.¹ *Id.* at 13:16–24. The patent explains that the FFT analysis of the aligned fibers may have adjacent “major peaks” (i.e., peaks higher than the average of peaks in the result) that are about 180° apart from each other.

Figure 8A, reproduced below, shows FFT analysis results for aligned fibers.

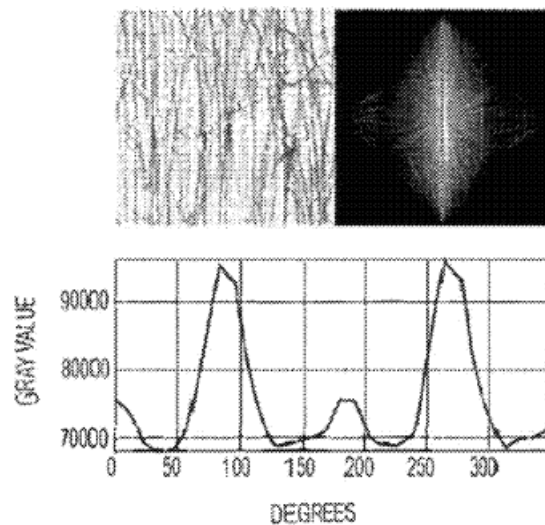


FIG. 8A

¹ Ayres et al., *Measuring fiber alignment in electrospun scaffolds: a user’s guide to the 2D fast Fourier transform approach*, 19 J. Biomater. Sci. Polymer. 603-621 (2008) (“Ayres 2008”; Ex. 1010). Petitioner’s expert, Dr. David G. Simpson, is named as an author of the Ayres 2008 article.

The top left image above shows electrospun fibers taken using a scanning electron microscope (SEM). *Id.* at 21:11–31. The top right image above shows the Fourier spectra of that SEM image created using the “ImageJ64 FFT tool” reflecting a known pattern for aligned fibers. *Id.* at 21:27–31. The same images are shown in Figure 3 of the ’223 patent. The graph below those two images is a 2-dimensional FFT plot of the Fourier spectra image, showing major peaks at about 90° and 270° (i.e., about 180° apart). The ’223 patent also includes comparative images and 2D-FFT plots for a control sample of randomly oriented fibers, where the major peaks are about 90° apart. *Id.* at Fig. 8B.

The ’223 patent indicates that a variety of natural or synthetic materials may be used alone or blended to form aligned fibers according to the electrospinning techniques described therein. *Id.* at 7:10–30. The examples in the patent utilize polycaprolactone (PCL) blended with heart basement membrane (HBM). *Id.* at 19:40–22:48. The claims of the ’223 patent, however, focus on collagen fibers.

2. *Illustrative Claim*

Petitioner challenges claims 1–12 of the ’223 patent. Claim 1 is the sole independent claim, and is representative for purposes of our analysis:

1. A scaffold comprising one or more electrospun fibers comprising collagen, wherein a fast Fourier transform (FFT) analysis result of the fibers ha[s] adjacent major peaks. . . about 180° apart from each other.

Ex. 1001, 23:6–9. Dependent claim 4 further specifies that the scaffold has an average porosity of from about 60% to about 90%. *Id.* at 23:14–15.

E. Prior Art and Asserted Grounds

Petitioner asserts that claims 1–12 would have been unpatentable on the following grounds:

Claim(s) Challenged	35 U.S.C. §²	Reference(s)/Basis
1–12	102	Huang2 ³
4	103	Huang2, Kumbar ⁴
1–12	102	Lee ⁵
1–12	103	Lee

Petitioner relies on the declaration of David G. Simpson, Ph.D (Ex. 1003). Patent Owner did not present an expert declaration with its preliminary response.

II. ANALYSIS

F. Discretionary Denial under 35 U.S.C. § 325(d)

Patent Owner filed a request for discretionary denial under 35 U.S.C. § 325(d). Paper 8. Petitioner opposed. Paper 10. The Acting Director denied the discretionary denial request. Paper 13 (June 26, 2025). Accordingly, we proceed with our analysis of the merits of Petitioner’s

² The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), amended 35 U.S.C. §§ 102 and 103. Because the ’223 patent claims priority to a provisional application filed before the effective date of the applicable AIA amendments (March 16, 2013), we refer to the pre-AIA versions of the statutes throughout this Decision.

³ 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 (Feb. 2012) (“Huang2”) (Ex. 1005). A different reference by Huang, identified as “Huang1” in the Petition, was considered by the Examiner during prosecution. Pet. 15–17; Ex. 1008.

⁴ Kumbar et al., *Electrospun nanofiber scaffolds: engineering soft tissues*, Biomed. Mater. 3 (2008) (“Kumbar”) (Ex. 1006).

⁵ Lee et al., U.S. Patent Application No. US 2010/0331980 A1, Pub. Date December 1, 2011 (“Lee”) (Ex. 1011).

patentability challenges and do not address the discretionary denial arguments presented by the parties.

G. Level of Ordinary Skill in the Art/Expert Qualification

Petitioner proposes that a person of ordinary skill in the art (“POSITA”) relevant to the ’223 patent “would be a Ph.D. student with a minimum of two years of experience in their faculty advisor’s laboratory” and would have an understanding of “electrospinning fibers, including for tissue engineering, tissue engineering techniques, and using/performing FFT analysis.” Pet. 18–19 (citing Ex. 1003 §II.C). Patent Owner does not dispute this skill level. Prelim. Resp. 10.

At this stage of the proceeding and for purposes of our analysis in this Decision, we adopt Petitioner’s definition as that definition is consistent with the level of skill in the art reflected by the prior art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required “where the prior art itself reflects an appropriate level and a need for testimony is not shown” (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

We further find that Petitioner’s expert is qualified to provide testimony from the perspective of a POSITA in this case. *See* Ex. 1003 ¶¶ 5–14 (describing Dr. Simpson’s qualifications); *Kyocera Senco Indus. Tools Inc. v. Int’l Trade Comm’n*, 22 F.4th 1369, 1377 (Fed. Cir. 2022) (“[T]o be qualified to offer expert testimony on issues from the vantage point of an ordinarily skilled artisan in a patent case, an expert must at a minimum possess ordinary skill in the art.”). Patent Owner does not challenge Dr. Simpson’s qualifications.

H. Claim Construction

We interpret a claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b) (2019). This standard requires that we construe claims “in accordance with the ordinary and customary meaning of such claim[s] as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *Id.*

Neither Petitioner nor Patent Owner proposes a construction for any claim terms. Pet. 19; Prelim. Resp. 10. We also do not perceive a need to construe any claim terms of the ’223 patent for purposes of determining whether to institute trial. *See Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 295, 803 (Fed. Cir. 1999) (holding that “only those terms need to be construed that are in controversy, and only to the extent necessary to resolve the controversy”); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review).

I. Overview of Asserted References

1. Overview of Huang2 (Ex. 1005)

Huang2 is a journal article that was first published online on December 2, 2011. Ex. 1005, 1791.⁶ It qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Pet. 21. Patent Owner does not dispute that Huang2 is available as prior art.

Huang2 studies collagen fibers used for tissue-engineered skin grafts. Ex. 1005, 1791. In particular, Huang2 compares aligned (anisotropic) fibers

⁶ We refer to the native page numbers of the original publication rather than the page numbers added to the exhibits by Petitioner.

to non-aligned (isotropic) fibers with regard to their effect on the attachment and growths of normal human dermal fibroblasts (“NHDFs”). *Id.* To mimic the skin’s native extracellular matrix (“ECM”), Huang² discusses creating “stable” scaffolds of electrospun collagen fibers by either crosslinking or blending with other materials. *Id.* at 1791–92. Huang² uses a blend of type I collagen and polycaprolactone (PCL) for its scaffolds. *Id.* at 1792. Specifically, “[n]anofibrous matrices of PCL and Collagen at a weight ratio of 3:1. . . were fabricated using electrospinning previously described.” *Id.*

Huang² characterizes both isotropic and anisotropic PCL/collagen blends in several ways, including SEM and FFT analysis. With regard to the FFT analysis, Huang 2 teaches:

The orientation of electrospun nanofibers was determined using the ImageJ program (NIH) along with the Oval Profile Plot plugin [22⁷]. Briefly, representative SEM images of the electrospun fibers were cropped into a square covering as much of the image as possible (the images used were 905 x 905 pixels I size). These cropped images were then processed with a fast Fourier transform (FFT) and then a circular section of the image was made maximizing the amount selected (edges of the circle were tangent with the edges of the image). This selection then underwent a radial summation using the Oval Profile Plot plugin with 360 points such that the degree interval was 1°. The raw data were normalized to 0 and data from all sets were rescaled to an arbitrary scale *versus* degrees, where the height of the peaks represents a greater degree of alignment at a given angle.

⁷ Reference [22] in Huang² is a publication entitled “*Modulation of anisotropy in electrospun tissue-engineering scaffolds: analysis of fiber alignment by the fast Fourier transform*” by Ayres et al. in *Biomaterials*, 2006; 27:5524–34 (“Ayres 2006”). Ex. 1005, 1800. Although not relied upon to teach any particular claim limitations, the Ayres 2006 and Ayres 2008 articles are discussed below give their relevance to Petitioner’s patentability challenges.

Id. at 1792.

These results are shown in Figure 1, reproduced below:

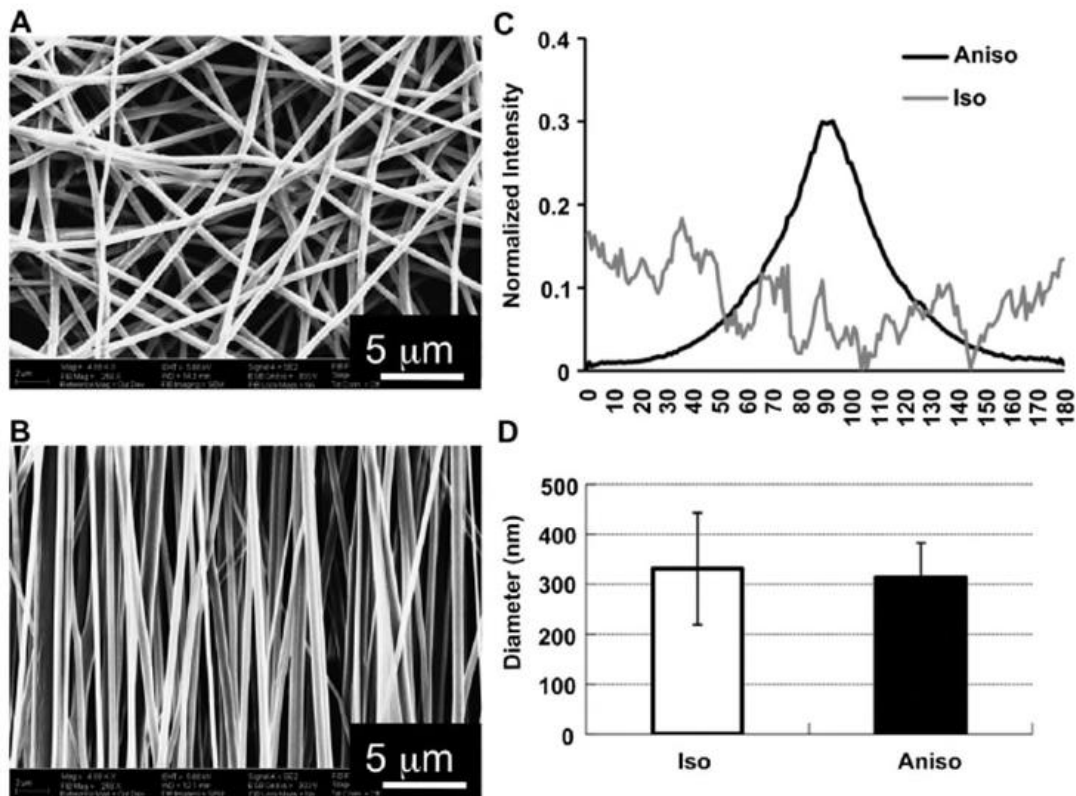


Figure 1A (top left) shows an SEM image of an isotropic sample of a PCL/Coll nanofibrous matrix, while Figure 1B (bottom left) shows an SEM image of an anisotropic (aligned) sample. Figure 1C (top right) shows the normalized intensity plots against the angle of acquisition for the isotropic and anisotropic samples obtained using FFT analysis. *Id.* at 1793.

Huang2's results showed that fibroblast-to-myofibroblast differentiation, important to the reconstruction of connective tissue during wound healing, was enhanced in the anisotropic PCL/collagen nanofibers due to the impact of the alignment on the integrin $\beta 1$ signaling pathway. *Id.* at 1797–99.

2. *Overview of Kumbar (Ex. 1006)*

Kumbar is a journal article published on August 8, 2008. Ex. 1006, 1. It qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Patent Owner does not dispute Kumbar's availability as prior art. Huang² (discussed above) cites Kumbar in its discussion of the desirable properties of electrospun scaffolds. Ex. 1005, 1799 (reference [3]).

Kumbar describes research efforts in “designing nanofiber matrices as scaffolds in the regeneration of various soft tissues including skin, blood vessel, tendon/ligament, cardiac patch, nerve and skeletal muscle.” Ex. 1006, 1 (Abstract). Kumbar notes that “electrospun nanofiber matrices have gained a lot of attention, and are being explored as scaffolds in tissue engineering due to their properties that can modulate cellular behavior.” *Id.* In preparing the electrospun fibers, Kumbar discloses the benefits of using collagen, explaining that “[c]ollagen nanofibers play a dominant role in maintaining the biological and structural integrity of various tissues and organs, including bone, skin, tendon, blood vessels and cartilage.” *Id.* at 7.

Kumbar also discloses desirable mechanical properties of scaffolds in tissue engineering. According to Kumbar, these properties are important “to provide cells with the necessary chemical cues and a more in vivo like environment” for use “in the regeneration of various soft tissues including skin[.]” *Id.* at 1 (Abstract). Kumbar describes that “[f]iber alignment in nanofiber matrices significantly improves the mechanical properties.” *Id.* at 6. Kumbar further explains that “[n]anofiber matrices as tissue engineering scaffolds need to have interconnected highly porous structures to facilitate cellular migration and transport of nutrients, and metabolic wastes to allow the formation of new tissue.” *Id.* With respect to “[e]lectrospun nanofiber

skin grafts,” Kumbar notes that “[c]ross linking collagen nanofibers resulted in decrease of porosity from 89% to 71%.” *Id.* at 7.

3. Overview of *Lee* (Ex. 1011)

Lee was published on December 30, 2010. Ex. 10011, code (43). It qualifies as prior art under Pre-AIA 35 U.S.C. § 102(b). Patent Owner does not dispute *Lee*’s availability as prior art.

Lee is generally directed an aligned scaffolding system for skeletal muscle regeneration. *Id.*, code (54) (title). *Lee* teaches that the reconstruction of skeletal muscle tissue due to a traumatic injury is difficult because of “the lack of available functional muscle tissue substitutes.” *Id.* at [0003]. To solve this problem, *Lee* describes engineered muscle tissue, including “a biodegradable scaffold comprising a plurality of fibers oriented along a longitudinal axis of the fibers” and “methods of forming a biodegradable scaffold, including the steps of electrospinning a solution comprising a biodegradable scaffold material onto a grounded mandrel to form a plurality of fibers oriented along a longitudinal axis; and crosslinking said fibers to form the scaffold.” *Id.* at [0005]–[0006]. *Lee* explains that its “[s]caffold” refers to an array of natural or synthetic matrix molecules to which cells or fibers can attach,” which may include various components and molecules. *Id.* at [0044].

Lee further describes using fibers for the scaffold that are natural, such as collagen, or synthetic, such as PCL, or blends of natural and synthetic fibers between 2:1 and 1:2 by weight. *Id.* at [0005]. *Lee* obtained electrospun nanofiber meshes “using a blend of PCL and collagen with a ratio of 1:1 in weight.” *Id.* at [0062]–[0063]. *Lee* explains that “PCL-collagen composite scaffolds according to some embodiments have

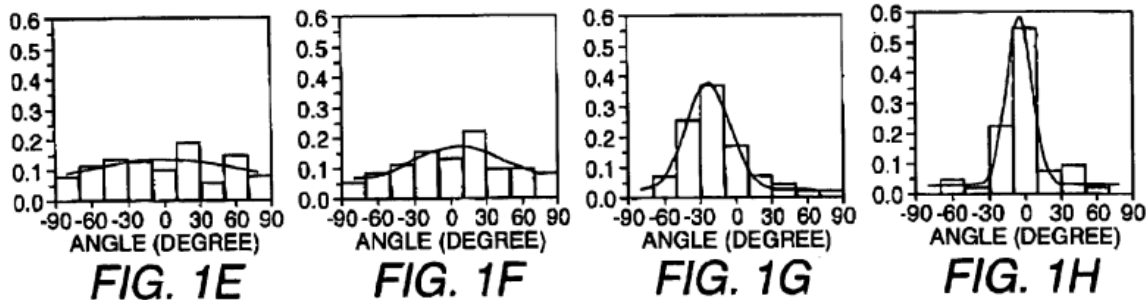
preferable biomechanical properties, e.g., yield tensile strength, elasticity and compliance.” *Id.* at [0052]. Lee teaches that when PCL and collagen are used together, “the mesh can be improved biocompatibility, mechanical properties, and processability,” and further explains that “in some embodiments the biomechanical properties of PCL-collagen scaffolds are similar to that of native tissue.” *Id.*

Further, to approximate skeletal muscle, Lee fabricated “nanofiber meshes that are aligned in a unidirectional manner to facilitate myotube formation.” *Id.* at [0090]. Lee explains that previous studies demonstrated that “aligned nanofibrous structures can be obtained using a variety of collecting mandrel systems, including rotating drum.” *Id.* at [91]. Lee discovered that “[f]iber alignment had a profound effect on the mechanical properties of electrospun PCL/collagen nanofiber meshes,” including increased tensile strength for the aligned nanofiber meshes. *Id.* at [0081].

Lee explains that the aligned fibers aided in cell growth—“[t]he myotubes that formed on the oriented nanofiber meshes showed unidirectionally organized myotubes that are consistently aligned along the longitudinal axis of nanofibers, which is in contrast to the randomly oriented nanofiber meshes (FIGS. 5c, f).” *Id.* at [0084]. While the “myotubes formed on the randomly oriented nanofiber meshes . . . did not show a global cellular organization,” Lee states that the “myotubes on the aligned nanofiber meshes organized within close proximity to the direction of the nanofiber direction and formed globally aligned myotubes (FIG. 6d).” *Id.* at [0085].

Lee obtained SEM images and plotted histograms of fiber angles for fibers that were electrospun at different rates of rotation. *Id.*, [0011].

Figures 1E–1H of Lee are reproduced below:



The figures above show normalized histograms of fiber angles obtained at different rates of rotation, ranging from “static” (Fig 1E on the left) to 2350 rpm (Fig. 1H on the right). As shown above, a distinct peak occurs in the histogram for fibers obtained at higher rates of rotation, which reflects the fiber orientation at that angle.

Lee concludes that the “[a]ligned nanofibers greatly influenced muscle cell organization and enhanced myotube formation,” and that “myotubes formed on the aligned nanofiber meshes were highly organized and were significantly longer than that of the myotubes on the randomly oriented meshes.” *Id.* at [0094]. “These findings indicate that the electrospun PCL/collagen nanofiber meshes are able to guide and orient skeletal muscle cells into organized structures that mimic native tissues.” *Id.*

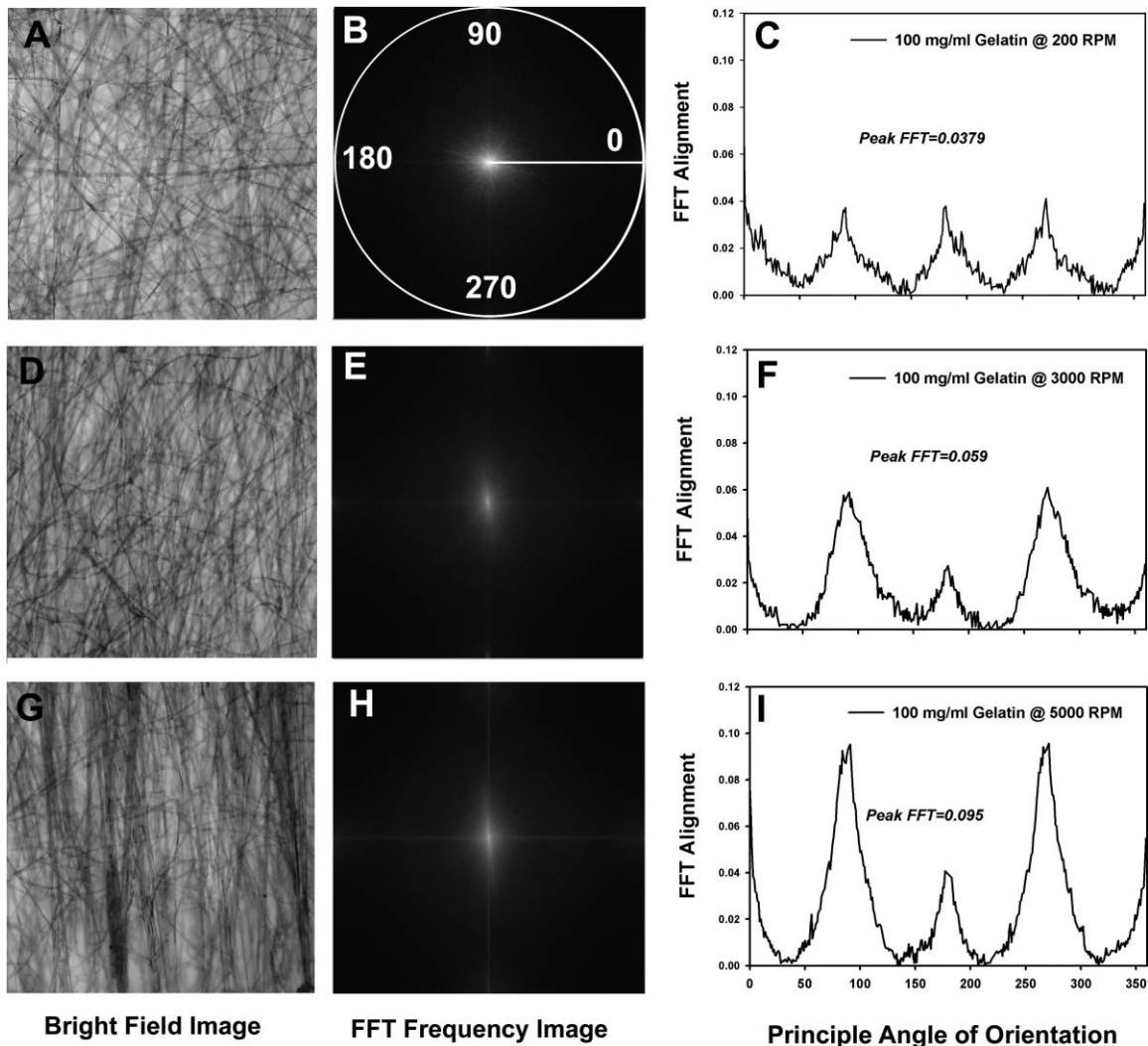
4. Overview of Ayres 2008 (Ex. 1010)

Ayres 2008 is an article published in the journal *Biomaterials* in 2008, and was later published online on April 2, 2012. Ex. 1010, 604. As noted above, Ayres 2008 was incorporated by reference into the ’223 patent. Ex. 1001, 13:17–24. Petitioner’s expert Dr. Simpson is one of the named authors of Ayres 2008. Patent Owner does not dispute that Ayres 2008 qualifies as prior art.

Ayres 2008 describes a method of using two-dimensional fast Fourier transform (2D FFT) to measure fiber alignment in electrospun materials.

Ex. 1010, 604. As explained in Ayres 2008, “[a] data image of an electrospun scaffold is composed of pixels that depict the spatial organization of the constituent fibers.” *Id.* The 2D FFT function converts this spatial information into a mathematically defined frequency domain that maps the rate at which pixel intensities change across the original data image,” which thereby “provides quantitative information concerning the orientation of objects in a data image.” *Id.*; see also *id.* at 608. ImageJ software (obtained from the NIH) supported by an oval profile plug-in was used to conduct the 2D FFT analysis. *Id.* at 607.

Figure 1 of Ayres 2008 is reproduced below:



Figures 1A, 1D, and 1G on the left show brightfield images of representative electrospun scaffolds composed of fibers with varying degrees of alignment. Figures 1B, 1E, and 1H in the middle show the ImageJ-generated “frequency plots,” while Figures 1C, 1F, and 1I on the right show the “2D FFT alignment plots” for the corresponding brightfield images.

As explained in Ayres 2008, “[w]hen an image of random fibers is processed by 2D FFT, the resulting frequency plot contains a cluster of white pixels that are concentrated in a symmetrical, circular pattern around the origin (Fig. 1B).” *Id.* at 609. On the other hand, the frequency plot for an image of aligned fibers will contain pixels “concentrated along a specific axis” (Figs. 1E, 1H). *Id.* at 610. After rotating the frequency plot by 90°, the intensities of the pixels are summed along the radius for each angle of a circular projection (0–360°) placed on the image using the ImageJ software. *Id.* at 609. The summed pixel intensities are then plotted against the corresponding angle to produce the 2D FFT alignment plot. Although Figures 1C, 1F, and 1I show the alignment data for the full 360° projection, Ayres 2008 notes that “[t]ypically, the data from this analysis is reported for 0 to 180°” because “the frequency plot is symmetric so a complete summation from 0 to 360° is not technically necessary.” *Id.*

As depicted in Figure 1C, “[t]he 2D FFT alignment plot of a random matrix will exhibit 4 peaks that occur every 90°.” *Id.* By contrast, “[t]he 2D FFT alignment 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. Ayres 2008 explains that “[t]he degree of alignment present in the original data image is reflected by the height and overall shape of the most prominent peaks present in the alignment plot.” *Id.*

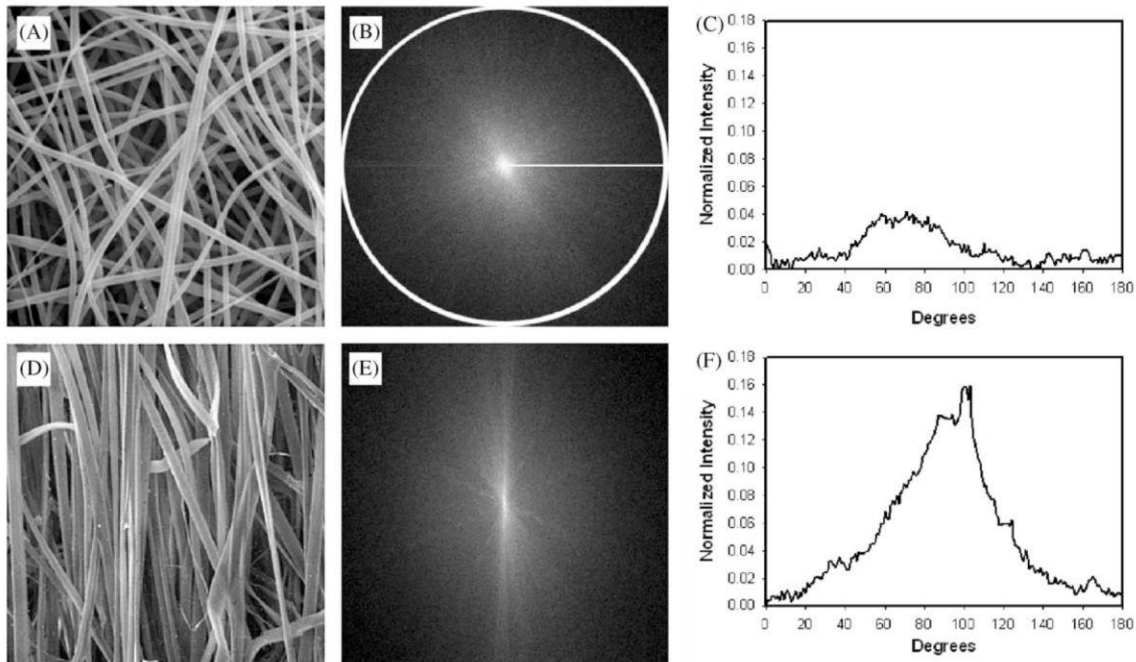
5. *Overview of Ayres 2006 (Ex. 1013)*

Ayres 2006 is an article published in the journal *Biomaterials* in 2006, and was later available online at PubMed Central (PMC) in 2010. Ex. 1013, 1. It names several of the same authors as Ayres 2008, including Petitioner's expert Dr. Simpson. As noted above, Huang² cites Ayres 2006 as the source for the FFT methodology used therein. Ex. 1005, 1800. Patent Owner does not dispute Ayres 2006's availability as prior art.

Ayres 2006 describes the use of FFT in the measurement of anisotropy in electrospun scaffolds of gelatin. Ex. 1013, 1. Ayres 2006 notes that "[b]y using FFT to assign relative alignment values to an electrospun matrix it is possible to systematically evaluate how different processing variables impact the structure and material properties of a scaffold." *Id.*

Ayres 2006 describes an FFT process similar to Ayres 2008 to quantify the degree of fiber alignment. As explained in Ayres 2006, "[t]he FFT function converts information present in an original data image from 'real' space into mathematically defined 'frequency' space," with "[t]he resulting FFT output image contain[ing] grayscale pixels . . . distributed in a pattern that reflects the degree of fiber alignment present in the original data image." *Id.* at 3. According to Ayres 2006, "[a] graphical depiction of the FFT frequency distribution can be generated by placing a circular projection on the FFT output image and conducting a radial summation of the pixel intensities for each degree between 0° and 360°, in 1° increments." *Id.* at 4. Once these summations are obtained, the pixel intensities were plotted between 0 and 180°. *Id.* Ayres 2006 notes that because "the FFT is symmetric about the horizontal axis . . . a pixel summation to 360° is unnecessary." *Id.*

Using this methodology, Ayres 2006 presents the results of an FFT analysis for a subjectively judged “random” matrix and an “aligned” matrix in Figure 1, reproduced below:



Id. at 12. The images above depict, from left to right, the SEM images of a random (A) and aligned (D) matrix, the corresponding “FFT output images” (B and E), and the resulting “pixel intensity plots” (C and F). *Id.* As shown above, the FFT output image for the aligned matrix contains pixels distributed in a “non-random, elliptical distribution” compared to the “symmetrical, circular shape” for the FFT output image of the random matrix. *Id.* at 3–4. “This distribution occurs because the pixel intensities are preferentially distributed with a specific orientation.” *Id.* at 4. The pixel intensity plot for the aligned matrix shows a distinct peak around 90°, with the height and overall shape of the peak reflecting the degree of alignment. *Id.*

J. Analysis of Ground 1: Anticipation by Huang2

In Ground 1, as presented in the Petition, Petitioner asserts that claims 1–12 are anticipated by the teachings of Huang2. Pet. 28–44. As explained in our analysis below, we find that Petitioner has demonstrated a reasonable likelihood of prevailing as to at least some of the challenged claims based on this ground. Our conclusion with regard to this ground is sufficient for institution based on all of the grounds identified in the Petition. *See SAS Inst., Inc. v. Iancu*, 584 U.S. 357, 370 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition”). We nonetheless address the remaining grounds of the Petition further below to provide some additional guidance for the parties during trial.

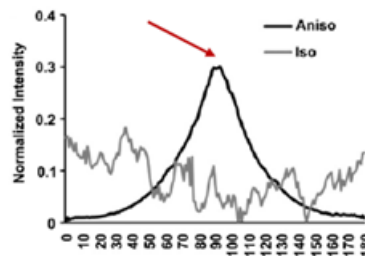
1. Independent Claim 1

Claim 1 requires a “scaffold” comprising “one or more electrospun fibers comprising collagen...wherein a fast Fourier transform (FFT) analysis result of the fibers have adjacent major peaks with about 180° apart from each other.” Ex. 1001, cl. 1. With regard to the “scaffold” requirement, Petitioner points to the teaching in Huang2 of “scaffolds [that] not only . . . provide a surface for cells to reside, but also . . . define a cell-friendly microenvironment that maximally recaptures the native extracellular matrix (ECM).” Pet. 28 (citing Ex. 1005, 1791). Patent Owner does not dispute that this element is taught by Huang2. Prelim. Resp. 12. We agree with Petitioner that this claim element is disclosed by Huang2.

With regard to the requirement of “electrospun fibers comprising collagen,” Petitioner points to the teaching in Huang2 of forming

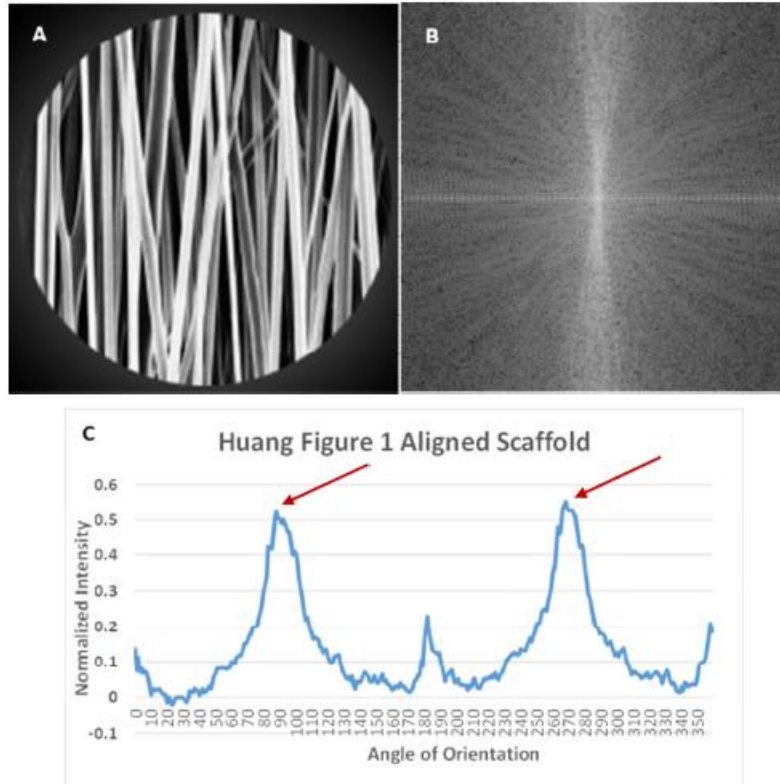
“[n]anofibrous matrices of PCL and Collagen” by “[e]lectrospinning a blend solution of collagen and polycaprolactone (PCL) [that] can yield rather stable nanofibers.” Pet. 28–29 (citing Ex. 1005, 1791–92). Patent Owner does not dispute that this element is taught by Huang2. Prelim. Resp. 12. We agree with Petitioner that this claim element is disclosed by Huang2.

With regard to requirement that the fibers exhibit an FFT analysis result having “adjacent major peaks with about 180° apart,” Petitioner points to Huang2’s description of the fibers shown in Figure 1B as “anisotropic” that were “aligned in the same direction.” Pet. 29–30 (citing Ex. 1005, 1792–94). Petitioner notes that Huang2 further confirmed the alignment of its PCL/Coll fibers through the use of FFT analysis, and that Huang2 uses the same ImageJ software used to perform the FFT analysis in the ’223 patent. Petitioner further notes that Figure 1C of Huang2 shows FFT results plotted from 0°–180° with a “major peak” around 90°, as reproduced blow:



Id. at 30. The figure above shows Huang2’s Figure 1C, annotated with a red arrow pointing to the major peak in the FFT plot for the anisotropic fibers (dark line). Petitioner acknowledges that Figure 1C only reports its results out to 180°, but contends that “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°.” *Id.* at 31 (citing Ex. 1010, 609).

Petitioner further relies upon Dr. Simpson's own FFT analysis of Huang2's Figure 1B. Pet. 31–32 (citing Ex. 1003 ¶¶ 110–111). Those FFT results are reproduced below:



Pet. 32. The image on the top left shows the SEM image of the aligned scaffold from Huang's Figure 1 after it had been cropped and masked for purposes of the 2D-FFT analysis. The image on the top right shows the 2D-FFT spectrum of the aligned scaffold after it was rotated to correct for the rotation intrinsic to the FFT analysis. The graph below those two images shows the normalized intensity values for the aligned scaffold shown from 0–360°, with the red arrows pointing to major peaks at about 90° and 270°. *Id.*

Patent Owner, in its preliminary response, argues that Huang2 does not expressly teach the FFT results required by the challenged claims because it only depicts a single major peak. Prelim. Resp. 15. Patent Owner

contends that Huang2's disclosure that the fibers are aligned is inapposite because the claims do not recite "aligned" fibers, but rather a specific FFT analysis result. *Id.* at 16. Patent Owner further argues that Petitioner does not clearly allege (much less clearly show) that the claimed FFT analysis result is inherently met by Huang2. *Id.* at 16–18.

Patent Owner also argues "Petitioner's contentions amount to an argument that a POSITA would have known (1) how to modify Huang2's single-peak FFT analysis result to double the length of its x-axis and plot the graph to 360° instead of 180° and (2) if they made such a modification, the POSITA would have expected to see 'adjacent major peaks with about 180° apart from each other.'" *Id.* at 19–20 (citing Pet. 31). Patent Owner contends that this argument is directed to obviousness, and does not demonstrate inherency of the claimed FFT analysis result. *Id.* at 21 ("Indeed, by arguing that Huang2 allegedly would show a second peak 'if the scale were extended,' Petitioner demonstrates that a second peak is not necessarily present in Huang2's FFT analysis result—the FFT analysis result would have to be modified to allegedly depict such a peak.").

Patent Owner appears to argue that Petitioner's evidence is insufficient to meet its burden for inherent anticipation. *Id.* at 21. Specifically, with regard to Dr. Simpson's testimony, Patent Owner argues that Petitioner cannot rely upon its expert to fill gaps in Huang2. *Id.* at 18–19. Patent Owner further contends that "Dr. Simpson's declaration does 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.'" *Id.* at 22 (citing *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (PTAB Aug. 24, 2022) (precedential)).

In addition, Patent Owner argues that the Ayres 2006 and Ayres 2008 papers cited by Dr. Simpson fail to provide independent corroboration or any further support for the contention that the FFT analysis is necessarily and always symmetric about the horizontal axis. *Id.* at 23–24. Patent Owner points out that the Ayres 2008 paper uses the qualifier “typically” when it states that “a complete summation from 0 to 360° is not technically necessary,” and this “casts doubt on whether adjacent major peaks are necessarily present.” *Id.* at 24. Patent Owner further argues that the Ayres 2008 paper undermines its own statement as to “typical” practice by presenting FFT results plotted to 360°. *Id.* Additionally, Patent Owner points out that the peaks at 90° and 270° shown in Figure 1A of Ayres 2008 have differences in shape and thus do not appear to be “repeats” of each other. *Id.*

With regard to the testing performed by Dr. Simpson, Patent Owner argues that Dr. Simpson failed to provide an explanation as to “[h]ow the test was performed and the data was generated” in violation of 37 C.F.R. § 42.65(b). Patent Owner contends that it is insufficient for Dr. Simpson to simply state that he conducted his own analyses “using the FFT analysis described in Huang2 and the ’223 patent,” and “report[ed] data from 0° to 360° and normalized the y-axis.” *Id.* at 26 (citing Ex. 1003 ¶ 110). Patent Owner points out that Huang2 and the ’223 patent employ FFT analysis described in different papers, so it’s unclear which specific methodology Dr. Simpson used. *Id.* at 27. Patent Owner points out that there are several critical aspects to the FFT methodology—including image type, compression, software version, illumination, light intensity, optical and electrical noise, and the use of masks—that Petitioner and Dr. Simpson fail

to account for, and thus “Dr. Simpson’s testing protocol is essentially unknown.” *Id.* at 27–31.

Based on the present record, we find that Petitioner has demonstrated a reasonable likelihood of establishing that the anisotropic fibers taught in Huang2 will necessarily have the claimed FFT analysis result with major peaks that are 180° apart. As noted by Petitioner, Huang2 includes an FFT analysis plot showing a major peak for the aligned fibers at 90°. The present record supports Petitioner’s contention that, if the same plot had been extended to 360°, it would necessarily show a second major peak at about 270°. The Ayres 2006 and Ayres 2008 papers both confirm that this symmetry is an inherent result of the FFT analysis for aligned (anisotropic) fibers. *See* Ayres 2008, 609 (“the frequency plot is symmetric so a complete summation from 0 to 360° is not technically necessary”). *See also* Ayres 2006, 4 (“the FFT is symmetric about the horizontal axis so a pixel summation to 360° is unnecessary”).

This symmetry is due to the inherent nature of the FFT analysis process. *Id.* As explained in the Ayres papers, the frequency plot for aligned fibers will exhibit pixels concentrated along a specific axis that reflects the alignment. Ayres 2008, 610 (“If a data image containing aligned fibers is processed by 2D FFT, the resulting frequency plot contains pixels that are concentrated along a specific axis.”); Ayres 2006, 4 (“[T]he FFT of a data image containing aligned fibers (Fig. 1D) results in an output image containing pixels distributed in a non-random, elliptical distribution (Fig. 1E).”). Given that the pixel intensities are summed along each degree between 0° and 360° to produce the plot, fibers aligned in the vertical (up and down) direction will have a concentration of pixels reflecting the alignment at around 90° and another concentration of pixels at around 270°

reflecting the same alignment in the opposite direction. See Ex. 1003 ¶ 108 (“[T]he fact that the FFT output image is symmetric about the horizontal axis (i.e., that the pixel intensity at 1° is the same as 181° , 2° is the same as 182° , etc.), means that the 2D FFT alignment plot repeats peaks every 180° .”). At this stage in the proceeding, we are not persuaded by Patent Owner’s arguments to the contrary. In particular, we do not find that Petitioner is improperly relying upon its expert to supply missing limitations in the prior art. Prelim. Resp. 18–19. Although prior art for *inter partes* reviews are limited to “patents and printed publications,” it is entirely appropriate for Petitioner to rely upon expert testimony to support a theory of inherency for a claimed feature not expressly disclosed in the prior art. Nor do we find that Petitioner’s arguments amount to an obviousness rationale rather than inherent anticipation rationale. Petitioner plainly contends that the FFT will produce a symmetrical plot “through its *inherent* mathematical properties,” and that “a [POSITA] would know that if the scale were extended to 360° , a second peak for the Aniso (aligned) sample would *necessarily* be at the symmetrical position of about 270° .” Pet. at 9, 22–23 (emphasis added). Contrary to Patent Owner’s characterization, the core issue is not whether it would have been obvious to extend the plot shown in Huang2 from 180° to the full 360° range, but rather whether the aligned fibers taught in Huang2 would inherently have an FFT analysis result with major peaks that are about 180° apart when such an analysis is extending another 180° .

We are also not persuaded by Patent Owner’s arguments against Dr. Simpson’s testimony at this preliminary stage. Dr. Simpson extensively discusses the FFT methodology used in the Ayres papers (for which he is the senior author), and we find these papers provide sufficient underlying facts,

data, and technical reasoning to support his opinion regarding the inherent symmetry of the FFT output image. Ex. 1003 ¶¶ 38–51. Contrary to Patent Owner’s argument, the fact that the Ayres 2008 paper uses the term “typically” does not undermine Dr. Simpson’s conclusion. Ex. 1010, 609. In context, it is clear that the referenced statement only speaks to how the data is typically reported rather than whether the result itself would only be typical. Indeed, the same sentence goes on to explain that the reason why the data is typically reported only for 0–180° is because “the frequency plot is symmetric.” *Id.* We are also not persuaded by Patent Owner’s argument that Ayres 2008 undermines Dr. Simpson’s testimony regarding “typical[] practice” because it presents FFT analysis results plotted to 360°. Rather than undermining his testimony, the plot shown in Figure 1F of Ayres 2008 further confirms the symmetrical nature of the FFT results for aligned fibers. Moreover, the fact that there are minor variations at the tips of the two peaks shown in Figure 1F does not undermine or contradict the conclusion that the major peaks for aligned fibers will necessarily be about 180° apart. The challenged claims do not require a perfect repetition or identity of the major peaks in the FFT output plot.

Additionally, Dr. Simpson’s own reproduced FFT analysis of the SEM image in Huang2’s Figure 1B using the methodologies described in the Ayres 2006 and Ayres 2008 papers, which shows major peaks at 90° and 270°, further confirms that the claimed FFT analysis result is an inherent feature of Huang2’s anisotropic fibers. Ex. 1003 ¶¶ 110–111. We do not find that Dr. Simpson’s testing violates 37 C.F.R. § 42.65(b), insofar as Dr. Simpson’s declaration sufficiently explains: (1) “why the test or data is being used”; (2) “how the test was performed and the data was generated”; (3) “how the data is used to determine a value”; (4) “how the test is regarded

in the relevant art”; and (5) “any other information necessary for the Board to evaluate the test and data.” See Ex. 1003 ¶¶ 38–51 (explaining FFT methodology used by Dr. Simpson). Although Dr. Simpson’s declaration does not appear to spell out all the details of the particular protocol or the version of the ImageJ software he used, we find his explanation that he used the methodology described in Huang2 (which references the Ayres 2006 paper) and the ’223 patent (which references the Ayres 2008 paper) sufficient for purposes of institution. Even assuming there may be some differences in the specific FFT methodology used in the two Ayres papers, we do not find anything at this stage to indicate that any such differences would matter with regard to the claim requirement that the major peaks are about 180° apart, especially given that both papers confirm the symmetrical nature of the FFT output plot. Furthermore, while Patent Owner argues that Dr. Simpson does not account for certain aspects of the FFT analysis discussed in the Ayres 2006 and Ayres 2008 papers, there is no evidence at this stage that Dr. Simpson did not follow the protocol described in his own papers, or that he failed to account for any specific aspects that could make a meaningful difference with regard to the FFT analysis result.

In view of the foregoing, we determine that Petitioner has established a reasonable likelihood of prevailing as to claim 1 based on this anticipation ground.

2. *Dependent Claims 2–12*

Dependent claim 2 recites that the “fibers comprise type I collagen in its native triple helix structure.” With regard to this claim, Petitioner points to Huang2’s teaching that “type I collagen” was used, and further that type I was well-known and generally understood to have a triple-helical form. Pet.

33 (citing Ex. 1005, 1792; Ex. 1017, 1, 9; Ex. 1003 ¶ 117). Patent Owner does not present any separate arguments for dependent claim 2. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 3 recites that the "fiber has less than about 8 wt % residual calcium." With regard to this claim, Petitioner points out that Huang2 does not indicate that any calcium was used when describing the materials used to prepare the nanofibers. Pet. 34 (citing Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 3. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 4 recites that the "scaffold has an average porosity from about 60% to about 90%." With regard to this claim, Petitioner points to Huang 2's teaching that "electrospun nanofibrous matrices characterized by ultrafine continuous nanoscaled fibers, high surface-to-volume ratio, *high porosity* and variable pore-size distribution, have great potential to mimic the skin ECM in both morphology and composition." Pet. 44 (citing Ex. 1005, 1791). Although Huang2 does not specify any particular percentage for the desired porosity level, Petitioner points out that Huang2 cites Kumbar (reference [3]) with respect the desired characteristics. *Id.* at 44–45 (citing Ex. 1005, 1799). Petitioner points out that Kumbar discloses that collagen type I has a porosity of 89%, which decreased to 71% when crosslinked. *Id.* at 45 (citing Ex. 1006, 7). Patent Owner does not present any separate arguments with regard to the anticipation challenge for dependent claim 2, but does argue against the combination of Huang2 and Kumbar for Ground 2 based on obviousness (discussed below). Prelim. Resp. 33–35. Based on the present record, we find that Petitioner is not

likely to prevail with regard to its anticipation challenge for dependent claim 4 based on Huang2 alone. As Petitioner recognizes, Huang2 does not explicitly disclose the claimed porosity levels. It is not clear that a skilled artisan would interpret Huang2's reference to "high porosity" to necessarily encompass the 89% or 71% porosity levels disclosed for type I collagen in Kumbar.

Dependent claim 5 recites that "the scaffold comprises collagen type I, bone matrix, adipose extracellular matrix, heart basement membrane extract, heart basement membrane extracellular matrix, placenta basement membrane extract, placenta basement membrane extracellular matrix, brain-derived extracellular matrix, polycaprolactone, an accessory polymer, or the mixture thereof." With regard to this claim, Petitioner points to Huang2's teaching that the scaffold can be made of a mixture of polycaprolactone (PCL) and type I collagen. Pet. 36 (citing Ex. 1005, 1792). Petitioner further points out the PCL disclosed in Huang2 qualifies as an "accessory polymer" (as defined in the '223 patent) because it is used to improve the stability and mechanical properties of the fibers. *Id.* at 36–37 (citing Ex. 1005, 1791–92). Patent Owner does not present any separate arguments for dependent claim 5. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 6 further limits claim 5, and recites:

wherein the accessory polymer is selected from the group consisting of polycaprolactone, poly(glycolic acid), poly(lactic acid), polydioxanone, poly(lactide-co-glycolide) copolymers, polyesters polysaccharides, polyhydroxyalkanoates, starch, polylactic acid, cellulose, proteins, agar, silks, alginate, collagen / gelatin, carrageenan, elastin, pectin, resilin, konjac, adhesives, gums, polyamino acids, polysaccharides, soy, zein, wheat gluten, casein, chitin / chitosan, serum albumin,

hyaluronic acid, lipids/surfactants, xanthan, acetoglycerides, waxes, surfactants, dextran, emulsan, gelian, polyphenols, levan, lignin, curd, ian, tannin, polygalactosamine, humic acid, shellac, pullulan, poly-gammaglutamic acid, elsinan, natural rubber, yeast glucans, synthetic polymers from natural fats and oils.

With regard to this claim, Petitioner once again points to Huang2's disclosure of PCL as an accessory polymer. Pet. 37 (citing Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 6. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 7 recites that the "scaffold comprise a bioactive factor." With regard to this claim, Petitioner points to Huang's disclosure of collagen, which is identified in the '223 patent as an exemplary "bioactive factor." Pet. 38 (citing Ex. 1001, 12:44–67; Ex. 1005, 1792). Petitioner further points out that Huang2 explains the proliferation of normal human dermal fibroblasts (NHDFs) on the bioengineered scaffolds. *Id.* at 38–39 (citing Ex. 1005, 1791). Patent Owner does not present any separate arguments for dependent claim 7. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 8 further limits claim 7 and recites:

wherein the bioactive factor is selected from the group consisting of an osteogenic growth factor, collagen, glycosaminoglycans, osteonectin, bone sialo protein, an osteoinductive factor, a chondrogenic factor, a cytokine, a mitogenic factor, a chemotactic factor, a transforming growth factor (TGF), a fibroblast growth factor (FGF), an angiogenic factor, an insulin-like growth factor (IGF), a platelet-derived growth factor (PDGF), an epidermal growth factor (EGF), a vascular endothelial growth factor (VEGF), a nerve growth factor (NGF), a neurotrophin, a bone morphogenetic protein (BMP), osteogenin, osteopontin, osteocalcin, cementum

attachment protein, erythropoietin, thrombopoietin, tumor necrosis factor (TNF), an interferon, a colony stimulating factor (CSF), stem cell derived factor-1 (SDF-1), and an interleukin.

With regard to this claim, Petitioner once again points to Huang2's disclosure of collagen as a bioactive factor. Pet. 39–40. Patent Owner does not present any separate arguments for dependent claim 8. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 9 recites that the “scaffold comprises an extracellular matrix component.” With regard to this claim, Petitioner points to Huang2's disclosure of collagen the extracellular matrix (ECM) component. Pet. 40–41. Petitioner points out that Huang2 teaches that “[c]ollagen fibrils” are a “major ECM component known for their mechanical properties” and that electrospun collagen fibers were fabricated “[t]o better mimic skin ECM.” *Id.* (citing Ex. 1006, 1791). Patent Owner does not present any separate arguments for dependent claim 9. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 10 further limits claim 9 and recites “wherein the extracellular matrix component is selected from the group consisting of collagen, glycosaminoglycans, osteocalcin, osteonectin, bone sialo protein, osteopontin, fibronectin, laminin, and mixtures thereof.” With regard to this claim, Petitioner once again points to Huang2's disclosure of collagen as the extracellular matrix component. *Id.* at 41. Patent Owner does not present any separate arguments for dependent claim 9. Based on the present record, we find that the evidence supports Petitioner's contentions regarding this claim.

Dependent claim 11 recites “[a] method of cell culture comprising culturing cells on the scaffold according to claim 1 under conditions suitable for the cell culture.” With regard to this claim, Petitioner points to Huang2’s teaching of culturing fibroblasts (NHDFs) on the isotropic and anisotropic nanofibrous matrices for up to 7 days. Pet. 41–42 (citing Ex. 1005, 1792). Petitioner also points to Huang2’s teaching of a wound healing assay, the results of which are shown in Figure 6 depicting the migration of human dermal fibroblasts on PCL/Coll nanofibrous matrixes. *Id.* at 42–43 (citing Ex. 1005, 1797 (Fig. 6A)). Patent Owner does not present any separate arguments for dependent claim 11. Based on the present record, we find that the evidence supports Petitioner’s contentions regarding this claim.

Dependent claim 12 further limits claim 11 and recites that “the cells are selected from the group consisting of stem cells, adipose derived stem cells, dental pulp stem cells, fibroblasts, and dorsal root ganglia.” With regard to this claim, Petitioner once again points to the disclosure in Huang2 about culturing fibroblasts on the nanofibrous matrices. Pet. at 43–44 (citing Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 12. Based on the present record, we find that the evidence supports Petitioner’s contentions regarding this claim.

K. Analysis of Ground 2: Obviousness of Claim 4 based on Huang2 combined with Kumbar

Claim 4 recites “an average porosity of from about 60% to about 90%.” In Ground 2, Petitioner asserts that claim 4, to the extent not anticipated for the reasons discussed above, would have been obvious over the combination of Huang2 and Kumbar. Pet. 44–47.

As discussed above, Huang2 discloses “high porosity” among the desirable characteristic of the electrospun nanofiber matrices, and further

cites Kumbar as a reference in support of these characteristics. Ex. 1005, 1791, 1799 (reference [3]). Kumbar discloses methods of designing electrospun nanofiber matrix scaffolds “to provide cells with the necessary chemical cues and a more in vivo like environment” for use “in the regeneration of various soft tissues including skin.” Ex. 1006, 1 (Abstract). Kumbar also states that a “high porosity” is desirable for these matrices as that property more closely approximates the natural ECM. *Id.* In terms of the specific amount of porosity, Petitioner once again points to Kumbar’s disclosure that collagen type I fibers had a porosity of 89%. *Id.* at 7. Kumbar also indicates that it can be useful to cross-link collagen type I nanofibers and that such crosslinked fibers were similar in strength to certain commercially available wound care products. *Id.* However, when these fibers were cross-linked, the porosity decreased to 71%. *Id.*

Petitioner contends that “a [POSITA] who desired to make aligned collagen blended fibers (as taught by Huang2) with ‘high porosity’ (as also taught by Huang2) would have been motivated to look at the reference cited by Huang2 in support of the ‘high porosity.’” Pet. 45–46 (citing Ex. 1003, ¶ 169). Accordingly, Petitioner contends that there would have been strong motivation to look to Kumbar’s teachings that collagen fiber scaffolds have a porosity of 89% or 71% (if crosslinked). *Id.* at 46 (citing Ex. 1006, 1, 6-7, 12; Ex. 1003, ¶ 169). Petitioner contends that both Huang2 and Kumbar are in the same field, involving the use of electrospun collagen-containing scaffolds for biomedical applications such as skin grafts. *Id.* (citing Ex. 1005, 1791; Ex. 1006, 1; Ex. 1003 ¶ 170). Petitioner also contends, based on Dr. Simpson’s testimony, that a POSITA would know how to tailor the porosity of electrospun fibers using well-known methods such as freeze-drying, salt leaching, and gas foaming. *Id.* at 46–47 (citing Ex. 1003 ¶ 171).

In response, Patent Owner contends that Huang² disclosed scaffolds made from a blend of collagen and PCL, whereas Kumbar only disclosed the porosity levels for pure collagen or cross-linked pure collagen. Prelim. Resp. 33–34. Patent Owner contends that given the differences in materials and properties of the materials used for the scaffolds in the two references, Petitioner has not demonstrated a motivation to apply the porosity levels disclosed by Kumbar for pure collagen to the blended fibers used in Huang², or a reasonable expectation of success in such a modification. *Id.*

Based on the present record, we find that Petitioner has demonstrated a reasonable likelihood of prevailing with regard to this obviousness challenge. We are not persuaded by Patent Owner’s arguments to the contrary at this stage. In particular, although Kumbar only discloses specific porosity levels for pure or cross-linked pure collagen, we find that Petitioner has demonstrated a motivation to combine the references because Huang² specifically cites Kumbar when discussing “high porosity” among the desirable properties for electrospun nanofibrous matrices. Moreover, in the absence of any evidence of unexpected results associated with the claimed porosity levels, the present record supports Petitioner’s contention that a POSITA would have a reasonable expectation of success in optimizing the porosity levels of Huang’s collagen/PCL blend to mimic the high porosity of native ECM, as also taught by Kumbar. *See In re Peterson*, 315 F.3d 1325,1330 (Fed. Cir. 2003) (“The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”).

*L. Analysis of Grounds 3 and 4: Anticipation or Obviousness
Based on Lee*

In Ground 3, Petitioner contends that claims 1–12 are anticipated by Lee. Pet. 47–64. In Ground 4, Petitioner contends that the same challenged claims are rendered obvious by Lee alone. *Id.* at 64–66. We discuss these grounds together, primarily with regard to independent claim 1.

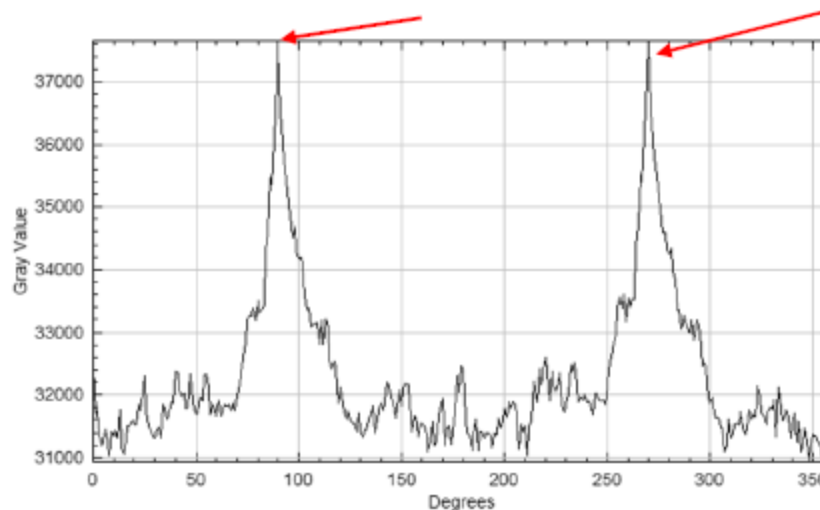
With regard to the “scaffold” requirement, Lee teaches “a biodegradable scaffold comprising a plurality of fibers oriented along a longitudinal axis.” Ex. 1011, Abstract; *see also* Pet. 46–47 (identifying teachings in Lee for a “scaffold”). Patent Owner does not dispute that this element is taught by Lee. We agree with Petitioner that this claim element is disclosed by Lee. Pet. 47–48.

With regard to the requirement for “one or more electrospun fibers comprising collagen,” Lee discloses “electrospun PCL/collagen nanofibers.” Ex. 1011, [0011]; *see also* Pet. 48–49 (identifying teachings in Lee related to electrospinning fibers to form PCL-collagen composite scaffolds). Patent Owner does not dispute that this element is taught by Lee. We agree with Petitioner that this claim element is plainly disclosed by Lee.

With regard to requirement that the fibers exhibit an FFT analysis result having “adjacent major peaks with about 180° apart,” Lee does not disclose any FFT analysis for its fibers. Petitioner, however, points to other teachings in Lee with regard to studying the impact of alignment and orientation of the electrospun PCL/collagen nanofibers on the performance and properties of the scaffolds. Pet. 49–52. In particular, Lee discloses that “fiber orientations were induced by electrospinning onto a collector at different rotation rates.” Ex. 1011, [0080]. Lee analyzed SEM images of the scaffolds with the “UTHSCSA ImageTool 3.0” to determine the average

fiber diameters and fiber orientations within the nanofiber meshes. *Id.*, [0066]. Because the SEM images in Lee have poor image quality, Petitioner points to images from Lee’s provisional application 61/025,350 (Ex. 1021) as showing the same data, but with clearer images. Pet. 50–51. Petitioner contends that the image analysis from these figures in the provisional application show that Lee discloses highly aligned fibers. *Id.* at 52.

Although Lee does not disclose an FFT analysis, Petitioner contends that a POSITA “would know that the degree of alignment could also be determined using ImageJ software to run an ‘FFT analysis.’” *Id.* Petitioner contends that this application of the ImageJ software was well known at the time of Lee’s filing, and the use of such an FFT analysis would confirm fiber alignment. *Id.* Petitioner further points to Dr. Simpson’s own FFT analysis based on Figure 1D of Lee’s provisional, which produced the following plot:



Pet. 5. Dr. Simpson explains that he conducted his own analysis of Lee’s Figure 1D using the FFT methodology identified in the ’223 patent (based on the Ayres 2008 paper), and reported the data from 0° to 360° as shown above. Ex. 1003 ¶ 189. As explained by Dr. Simpson, the graph above demonstrates that the aligned fibers have a first major peak at about 90° and

a second major peak at about 270° (annotated with red arrows), which shows the peaks are about 180° apart as recited in claim 1. *Id.* Dr. Simpson contends that these FFT properties are “naturally and necessarily present” in the aligned fibers disclosed in Lee, and that the fiber alignment was further confirmed in Lee through materials testing showing enhanced strength along the axis of alignment. *Id.* ¶¶ 190–91 (citing Ex. 1011, Fig. 9, [0052]).

With regard to the FFT limitation, Patent Owner presents many of the same arguments discussed above with regard to the anticipation ground based on Huang2. Prelim. Resp. 35–41. Patent Owner argues that Lee does not disclose any FFT results, and the mere disclosure of fiber alignment is insufficient to satisfy this limitation. With regard to Dr. Simpson’s FFT analysis of Figure 1D from Lee’s provisional application, Patent Owner highlights the poor image quality of the image used from Lee’s provisional application, and notes the importance of image quality in the FFT analysis. *Id.* at 39. Patent Owner also argues that Dr. Simpson failed to establish that he accounted for different variables in the FFT analysis, including image compression and storage type, calibration of the ImageJ software, uneven illumination, light intensity, optical and electrical noise, fiber array and any applied mask. *Id.* at 40–41.

With respect to these grounds, Petitioner does not clearly assert in the Petition that the fibers taught by Lee necessarily or inherently satisfy the FFT analysis requirement. Rather, Petitioner only asserts that “it was well known at the time of filing that an FFT analysis *could be* performed to further confirm alignment,” and “[t]his *would show* the fibers were oriented on the scaffold in Lee in an aligned manner.” Pet. 52 (emphasis added). Petitioner’s grounds based on Lee may ultimately fail on the merits due to this lack of specificity. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d

1356, 1363 (Fed. Cir. 2016) (“In an IPR, the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.”); 35 U.S.C. § 312(a)(3) (requiring that “the petition identifies in writing and *with particularity*, each claim challenged, the grounds on which the challenge to each claim is based, and the evidence that supports the grounds for the challenge to each claim”) (emphasis added).

We recognize that Lee does not disclose any FFT results, whereas Huang² at least disclosed an FFT analysis from 0–180° with a single major peak at 90°. Nonetheless, the present record (including Dr. Simpson’s testimony and the FFT analysis he conducted on Lee’s image) suggests that the “highly oriented” and “aligned” PCL/collagen fibers taught by Lee will satisfy the requirement of having an FFT analysis result with adjacent major peaks about 180° apart. At this stage, in the absence of any expert testimony to the contrary, we find no basis to question the methodology that Dr. Simpson followed in conducting his FFT analysis or the results he obtained showing two major peaks at 90° and 270° for Lee’s image.

We have also considered the obviousness challenge based on Lee alone, but do not reach a conclusion for this ground. We note, however, that both Petitioner’s and Patent Owner’s arguments regarding this obviousness challenge focus on whether there would be motivation and a reasonable expectation of success for a POSITA to run an FFT on the aligned fibers fabricated in Lee. Pet. 64–66; Prelim. Resp. 42–46. However, the challenged claims are directed to a scaffold, with the FFT analysis result recited as a *property* of the electrospun collagen fibers used in the scaffold. As such, we do not find it necessary for the prior art to have explicitly taught or motivated a POSITA to conduct an FFT analysis of the aligned fibers taught by Lee. See *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1347

(Fed. Cir. 1999) (“[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.”).

We have also considered Petitioner’s arguments and evidence regarding how dependent claims 2–12 are anticipated by Lee. Pet. 53–64. Patent Owner does not present any separate arguments for these dependent claims with regard to this anticipation challenge. At this stage, we find Petitioner’s contentions regarding these dependent claims appear to be supported by the cited teachings in Lee.

III.CONCLUSION

For the forgoing reasons, Petitioner has demonstrated a reasonable likelihood that at least one challenged claim of the ’223 patent would have been unpatentable over the prior art of record. Accordingly, we institute an *inter partes* review on all claims and all grounds set forth in the Petition.

IV.ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314, an *inter partes* review is instituted on all challenged claims and grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, *inter partes* review of the ’223 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

IPR2025-00248
Patent 10,137,223 B2

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