

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.

IPR2025-00249
Patent 11,318,227 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 1–8 of U.S. Patent Number 11,318,227 B2 (Ex. 1001, “the ’227 patent”). Paper 2 (“Petition” or “Pet.”). LifeNet Health (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 8 (“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 1–8 of the ’227 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 ’227 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 party-in-interest (“RPI”). Pet. 2. Petitioner further identifies Zimmer Biomet Holdings, Inc. (“ZBH”) as a second RPI “[o]ut o[f] an abundance of caution.” *Id.* at 3. 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 10,137,223 (“the ’223 patent”) in IPR2025-00248. We issue our institution decision in that proceeding concurrently with this decision.

D. The ’227 Patent (Ex. 1001)

1. Specification

The ’227 patent is titled “Aligned Fiber and Method of Use.” Ex. 1001, code (54). The ’227 patent issued from Appl. No. 16/045,159, which claims priority as a divisional of Appl. No. 14/776,106 filed March 13, 2014. *Id.* at codes (21), (62). The ’227 patent further claims priority to Provisional Appl. No. 61/785,031, filed on March 14, 2013. *Id.* at code (60).

The ’227 patent discloses a scaffold comprising an aligned fiber used for tissue engineering. *Id.* at 1:23–35. 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 2:24–7:63. 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 2:25–28. The electrified spinneret is used to extrude a polymer solution to form fibers. *Id.* at 3:18–41. 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 5:4–6. The fibers may be aligned in an angle ranging from about 90° to about 155° or less. *Id.* at 4:6–18.

The '227 patent further describes the use of fast Fourier transform (FFT) analysis to measure the degree of alignment of the electrospun fibers. *Id.* at 13:23–49. 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 '227 patent.¹ *Id.* at 13:39–45. 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. *Id.* at 13:25–29.

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

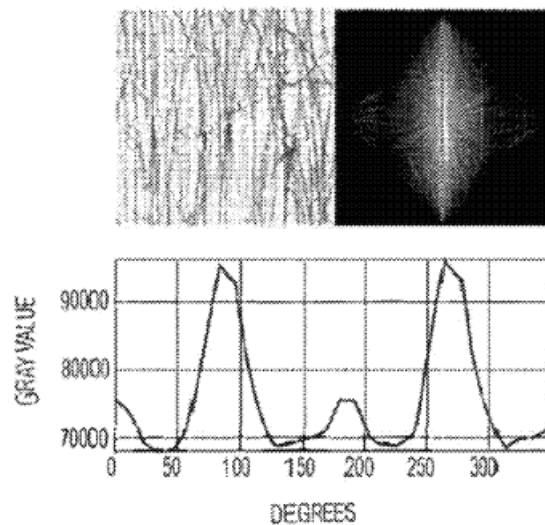


FIG. 8A

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 21:25–28. 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 21:40–45. The same images are shown in Figure 3 of the ’227 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 ’227 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 ’227 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 7:35–55. The examples in the patent utilize polycaprolactone (PCL) blended with heart basement membrane (HBM). *Id.* at 19:64–23:2.

2. *Illustrative Claims*

Petitioner challenges claims 1–8 of the ’227 patent. Claims 1 and 7 are independent claims and are reproduced below:

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.

Ex. 1001, 23:29–37.

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.

Id. at 24:5–11.

E. Prior Art and Asserted Grounds

Petitioner asserts that claims 1–8 would have been unpatentable on the
following grounds:

Claim(s) Challenged	35 U.S.C. §²	Reference(s)/Basis
1–6	103	Huang ² , Kuo ⁴
1–6	103	Lee, ⁵ Kuo
7, 8	102	Huang ²

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.

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. 16–18; Ex. 1008.

⁴ Kuo et al., U.S. Patent Application No. US 2011/0293685 A1, Pub. Date Dec. 1, 2011 (“Kuo”) (Ex. 1018).

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

II. ANALYSIS

A. *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 9. Petitioner opposed. Paper 9. The Acting Director denied the discretionary denial request. Paper 12 (June 26, 2025). Accordingly, we proceed with our analysis of the merits of Petitioner’s patentability challenges and do not address the discretionary denial arguments presented by the parties.

B. *Level of Ordinary Skill in the Art/Expert Qualification*

Petitioner proposes that a person of ordinary skill in the art (“POSITA”) relevant to the ’227 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. 20–21 (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.

C. 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 ’227 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).

D. 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 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

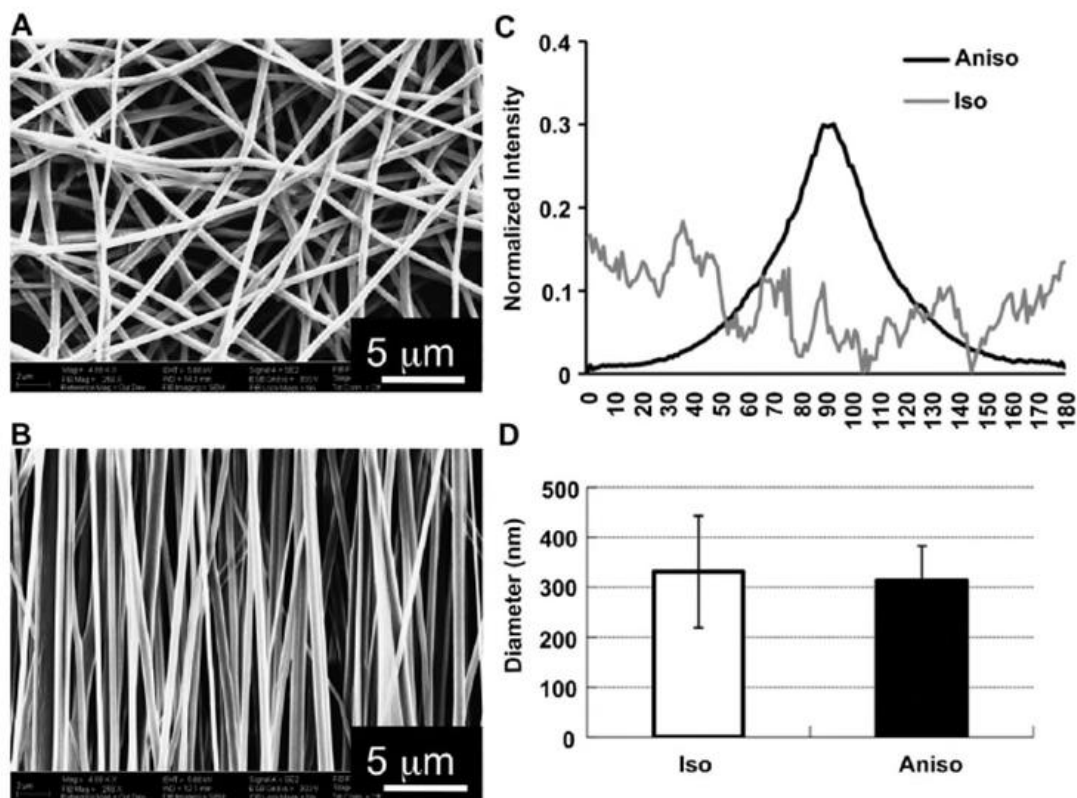
⁶ We refer to the native page numbers of the original publication rather than the page numbers added to the exhibits by Petitioner.

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

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.

Id. at 1792.

These results are shown in Figure 1, reproduced below:



2008 articles are discussed below give their relevance to Petitioner's patentability challenges.

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 Kuo (Ex. 1018)

Kuo was published on December 1, 2011. Ex. 1018, code (43). It qualifies as prior art under 35 U.S.C. § 102(b). Patent Owner does not dispute Kuo's availability as prior art.

Kuo, entitled "Scaffolds For Tissue Engineering And Regenerative Medicine," discloses electrospun collagen/PCL scaffolds for "tissue repair" that are seeded with cells and formed into a desired shape to replace tissue including muscles, *ligaments, tendons, and nerves*, among others. *Id.*, code (54), Abstract, [0005], [0052], [0113]. The scaffolds described in Kuo are created by electrospun micro or nano fibers with "fiber orientation that is random, *aligned*, or any combination thereof." *Id.*, [0005] (emphasis added). Kuo reports how their "[a]ligned nanofiber scaffolds were seeded with progenitor cells and subsequently rolled with the leading edge parallel to the axis of alignment." *Id.*, [0112]. Kuo explains that "[t]his aligned nanofiber scaffold locally mimicked the native microstructure of tendon/ligament (aligned collagen fibrils), globally mimicked a fascicle or

bundle in tendon/ligament tissue, and resulted in cell seeding throughout the construct.” *Id.*

Kuo further notes that the fibers may be comprised of natural materials (including collagen), synthetic materials, or a combination of both natural and synthetic materials. *Id.*, [0005], [0014]. Kuo describes the cells that can seed the scaffold as “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, hormonesecreting cells, neurons, tenocytes, skeletal myocytes, and skeletal myoblasts.” *Id.*, [0016], [0058]–[0066].

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.*

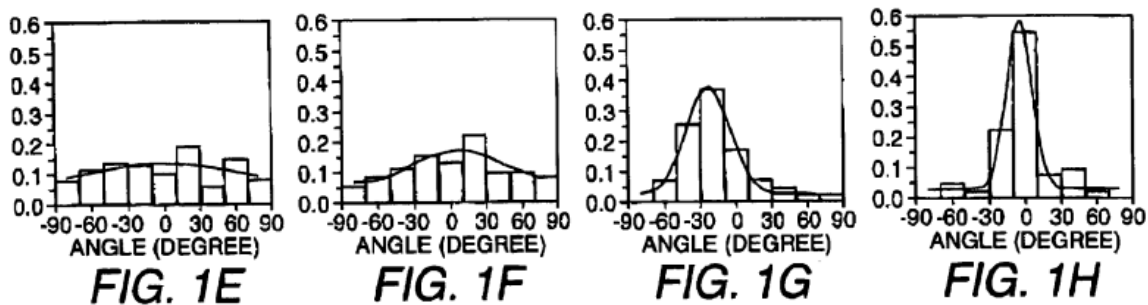
Further, to approximate skeletal muscle, Lee fabricated “nanofiber meshes that are aligned in a unidirectional manner to facilitate myotube formation.” *Id.* at [0090]. Lee explains that previous studies demonstrated that “aligned nanofibrous structures can be obtained using a variety of collecting mandrel 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.

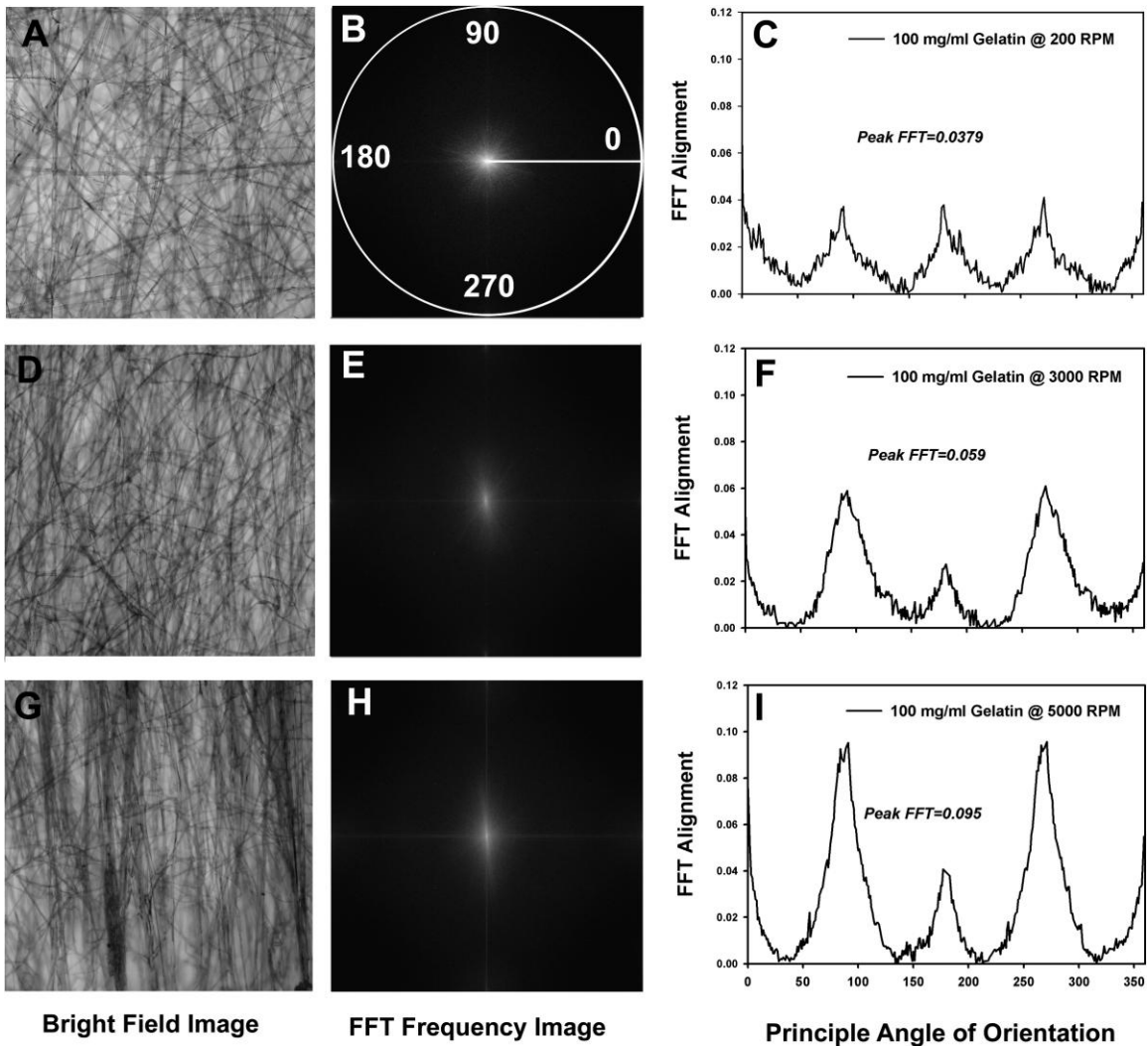
Lee concludes that the “[a]ligned nanofibers greatly influenced muscle cell organization and enhanced myotube formation,” and that “myotubes formed on the aligned nanofiber meshes were highly organized and were significantly longer than that of the myotubes on the randomly oriented meshes.” *Id.* at [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 '227 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)

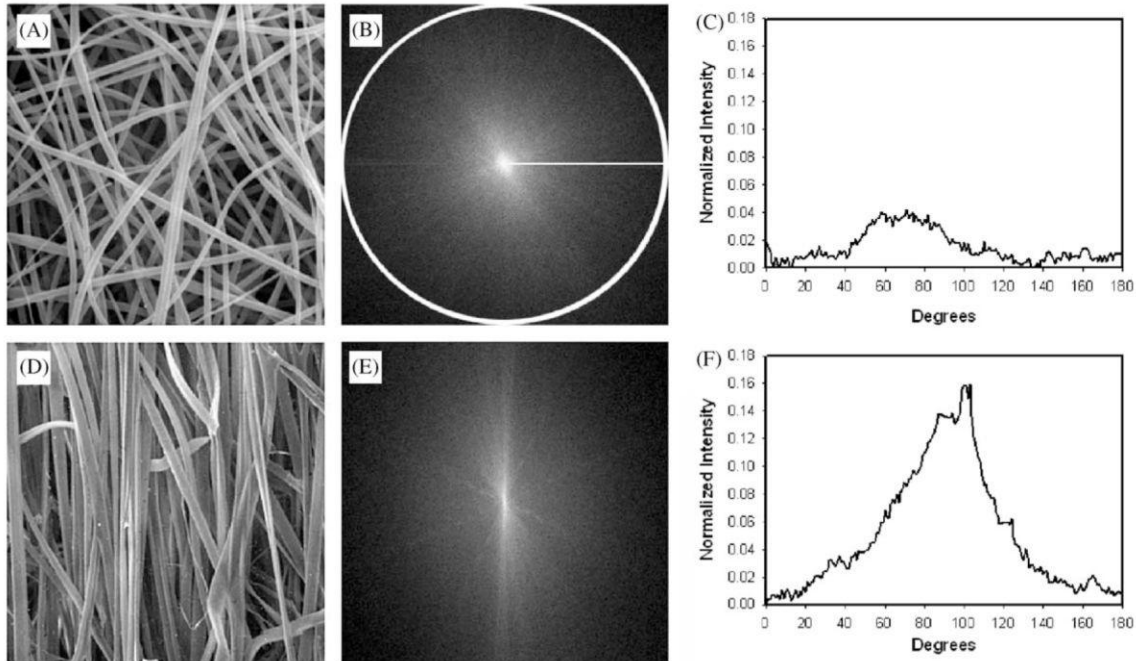
Ayres 2006 is an article published in the journal *Biomaterials* in 2006, and was later available online at PubMed Central (PMC) in 2010. Ex. 1013, 1. It names several of the same authors as Ayres 2008, including Petitioner’s expert Dr. Simpson. As noted above, Huang² cites Ayres 2006 as the source for 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:



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.* at 12. 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.*

E. Analysis of Ground 3: Anticipation of Claims 7 and 8 by Huang2

In Ground 3, as presented in the Petition, Petitioner asserts that claims 7 and 8 are anticipated by the teachings of Huang2. Pet. 59–63. As explained in our analysis below, we find that Petitioner has demonstrated a

reasonable likelihood of prevailing as to challenged claims 7 and 8 based on this anticipation ground. Our conclusion with regard to this ground is sufficient for institution of an *inter partes* review with respect to all challenged claims 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 as to claims 1–6 of the Petition further below to provide some additional guidance for the parties during trial.

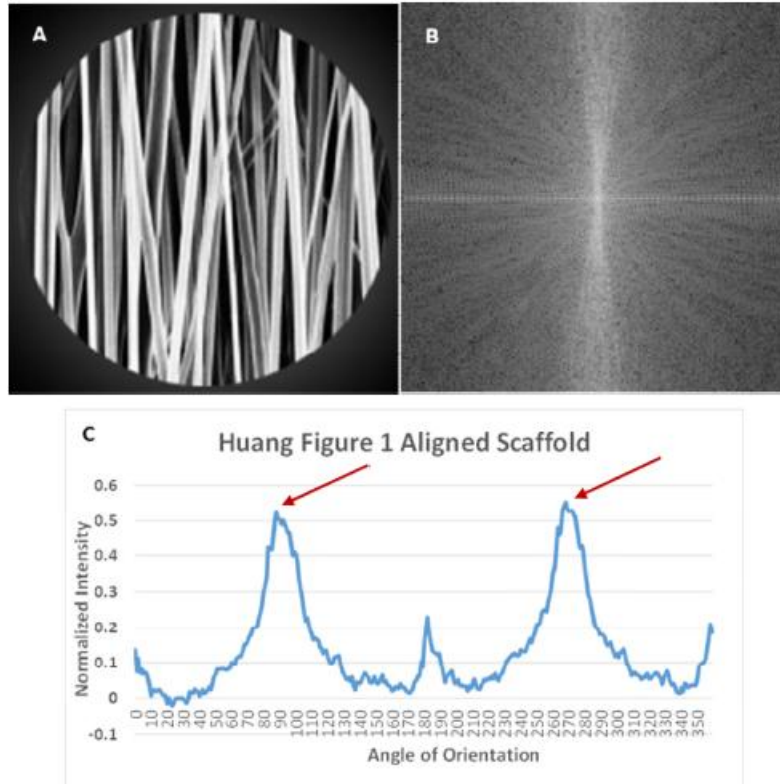
1. *Independent Claim 7*

Claim 7 recites “[a] method of cell culture comprising placing cells on a scaffold comprising aligned fibers.” Ex. 1001, cl. 7. Claim 7 further requires “growing the cells in conditions suitable for the cell culture.” *Id.* With regard to these requirements, Petitioner points to the teaching in Huang² that “[n]ormal human dermal fibroblasts (NHDFs) were seeded on collagen-containing PCL nanofibrous matrices with either isotropic nanofiber arrangement (i.e., randomly collected nanofibers with no alignment, abbreviated as ‘Iso’) or anisotropic nanofiber arrangement (i.e., collected nanofibers with alignment, abbreviated as ‘Aniso’).” Pet. 59 (citing Ex. 1005, 1792). Petitioner further points to Huang²’s disclosure of a wound healing assay performed by culturing cells on various matrixes to show the differences between cell growth observed on anisotropic and isotropic scaffolds. *Id.* at 61–62 (citing Ex. 1005, 1792, 1795–96, Figs. 2–7). Patent Owner does not dispute that these elements of claim 7 are taught

by Huang2. We agree with Petitioner that these claim elements are disclosed by Huang2.

Claim 7 further requires that “a result of a FFT analysis of the fibers demonstrate that the fibers have major adjacent peaks that are about 180° apart from each other.” With regard to this FFT analysis requirement, Petitioner points to the FFT analysis results shown in Figure 1C of Huang2, which was reported out to 180° showing a single major peak at about 90°. *Id.* at 60 (citing Ex. 1010, 609). Petitioner further relies upon Dr. Simpson’s testimony that a POSITA would know based on the alignment of the fibers depicted in SEM image of Figure 1B, and the major peak shown at around 90° in plot of Figure 1C, that there “would necessarily be a second peak about 180° apart at 270°.” *Id.* (citing Ex. 1003 ¶ 237).

Petitioner further relies upon Dr. Simpson’s own FFT analysis of Huang2’s Figure 1B. *Id.* (citing Ex. 1003 ¶¶ 125–26, 241–42). Those FFT results are reproduced below:



Ex. 1003 ¶ 243. 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.* ¶ 244.

In its preliminary response, Patent Owner's only argument against the anticipation challenge to claims 7 and 8 is that that Huang2 fails to disclose, either expressly or inherently, an FFT analysis result with major adjacent

peaks that are about 180° apart. Prelim. Resp. 57–58.⁸ 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 not taught by Huang2. *Id.* at 16. Patent Owner further argues that 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, but Petitioner does not identify either theory with specificity. *Id.* at 18–19. To the extent that a modification is required, Patent Owner argues that Petitioner fails to present a motivation to modify Huang2’s FFT analysis result, which is plotted to only 180°, to instead plot the graph to 360°. *Id.*

Even assuming that a POSITA would have reported the FFT results of Huang2 to 360°, Patent Owner contends that Petitioner’s evidence is insufficient to show that major adjacent peaks that are about 180° apart would inherently exist. *Id.* With regard to Dr. Simpson’s testimony, Patent Owner argues that prior art in an *inter partes* review is limited to “patents and printed publications,” and thus Petitioner cannot rely upon its expert to fill gaps in Huang2. *Id.* at 17–18. Patent Owner further contends that Dr. Simpson’s testimony is conclusory, and does not disclose underlying facts, data, or technical reasoning to support his conclusion regarding the symmetry of the 2D FFT output image. *Id.* at 19–20 (citing 37 C.F.R. § 42.65(a); *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15 (PTAB Aug. 24, 2022) (precedential); *Honeywell Int’l Inc. v. 3G Licensing*,

⁸ Patent Owner presents the same arguments with regard to the FFT analysis requirement in claim 1 of the ’227 patent, as well as in the claims of the related ’223 patent challenged in IPR2025-00248.

S.A., 124 F.4th 1345, 1354 n.6 (Fed. Cir. 2025). Accordingly, Patent Owner argues that Dr. Simpson's testimony should be given little or no weight. *Id.*

Patent Owner also 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 21–22. 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 22. Patent Owner further argues that the Ayres 2008 paper undermines Dr. Simpson's testimony as to what is the “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.* at 22–23.

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). *Id.* at 23–24. 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 24 (citing Ex. 1003 ¶ 125). 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 24–25. 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 25–29.

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”); 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. 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 ¶ 241 (“[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°.”).

We are not persuaded by Patent Owner’s arguments to the contrary at this stage. In particular, we do not find that Petitioner is improperly relying upon its expert to supply missing limitations in the prior art. 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 relies upon an obviousness theory to satisfy the FFT analysis requirement. 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, 227 (emphasis added). Contrary to Patent Owner’s framing of the issue, the FFT analysis result is merely recited as a *property* of the electrospun collagen fibers used in the claimed scaffold. As such, it is not necessary for the prior art to have explicitly taught or motivated a POSITA to extend the normalized intensity plot in Huang2’s Figure 1C to the full 360° range in order to find this property satisfied by Huang2’s aligned fibers. 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 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. As such, we do not find his testimony to be conclusory in violation of 37 C.F.R. § 42.65(a).

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 the 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 ¶¶ 125–26, 243–44. 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 Huang 2 (which references the Ayres 2006 paper) and the '223 patent (which references the Ayres 2008 paper) is 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 7 based on this anticipation ground.

2. *Dependent Claim 8*

Dependent claim 8 recites that the “cells are stem cells, adipose derived stem cells, dental pulp stem cells, fibroblasts, and/or dorsal root ganglia.” Ex. 1001, cl. 8. With regard to this claim, Petitioner points to Huang2’s teaching that fibroblasts were grown on the aligned collagen/PCL scaffolds. Pet. 62–63 (citing Ex. 1005, 1792. 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.

F. *Analysis of Ground 1: Obviousness of Claims 1–6 based on Huang2 combined with Kuo*

In Ground 1, Petitioner contends that claims 1–6 would have been obvious based on the combination of Huang2 and Kuo. Although we have already made a determination to institute an *inter partes* review on all grounds set forth in the Petition, we provide some guidance to the parties with regard to this ground below. We focus our discussion of this ground on the issues raised with regard to independent claim 1.

Independent claim 1 recites “[a] method of treating a tissue defect in a subject comprising implanting at the tissue defect a scaffold comprising crosslinked fibers comprising collagen.” Ex. 1001, cl. 1. Petitioner contends that Huang2 itself describes this claim element. Pet. 33. In particular, Petitioner points to Huang2’s teaching of nanofibrous matrices made from a blend of PCL and collagen, and that “crosslinking” can be used

to “obtain a stable scaffold.” *Id.* (citing Ex. 1005, 1791–92). Petitioner further points to Kuo’s teaching of an electrospun blend of PCL:collagen type I. With regard to the crosslinking requirement, Petitioner points to Kuo’s incorporation by reference a paper by Meinel, et al., 2004, *Biotechnol. Bioeng.* 88:379-391 (Ex. 1023), regarding preparation of the scaffold from electrospun fibers. *Id.* at 33–34 (citing Ex. 1018, [0040]). As noted by Petitioner, Meinel teaches that crosslinking can decrease the rate of collagen degradation by two orders of magnitude. *Id.* at 34 (citing Ex. 1023, 380–81, 390). Petitioner contends that “a skilled artisan would have been motivated with a reasonable expectation of success to utilize Huang2’s aligned fibers to create a scaffold that can treat a tissue defect, and would have been motivated to improve the stability of collagen fibers by chemically crosslinking, as taught by both Huang2 and Kuo.” *Id.*

With regard to the requirement that the collagen fibers are crosslinked, Patent Owner argues that Huang2 only teaches that “*either crosslinking or combination with other materials is necessary to obtain a stable scaffold,*” and that Huang2 elected to utilize a blend of collagen and PCL and did not utilize a scaffold with crosslinked fibers. Prelim. Resp. 30–31. Furthermore, Patent Owner argues that Meinel only teaches crosslinking pure collagen, and does not crosslink a PCL/collagen blend like Huang2. *Id.* Patent Owner argues that Petitioner did not rely upon Dr. Simpson’s testimony as to motivation to improve stability by crosslinking and that, in any event, this testimony is conclusory and unsupported. *Id.* at 31–32 (citing Ex. 1003 ¶ 114).

Based on the present record, we find that Petitioner has sufficiently shown that a POSITA would have been motivated to use crosslinked collagen fibers in a scaffold for tissue engineering. Although Huang2

specifically chose to conduct its experiments and analysis with a collagen/PCL blend rather than crosslinked collagen, that does not detract from Huang2's teaching of crosslinking as one method to improve stability of the scaffold. "[T]he fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered." *Merck & Co. v. Biocraft Lab'ys, Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (citing *In re Lamberti*, 545 F.2d 747, 750 (CCPA 1976)); see also *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) ("The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed."). Furthermore, we find that the present record supports Petitioner's contentions that a POSITA would have been motivated to crosslink collagen fibers based on Meinel's teaching that crosslinking reduced the rate of degradation of collagen fibers. Contrary to Patent Owner's unsupported arguments, we find no basis on the present record to suggest that that a POSITA would find the benefits of crosslinking recognized in both Huang2 and Meinel to be applicable for only scaffolds containing pure collagen rather than PCL/collagen blends.

Claim 1 further recites "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." Ex. 1001, cl. 1. Petitioner and Patent Owner rely upon the same arguments concerning this FFT analysis limitation discussed above with regard to the similar limitation recited in independent claim 7. See Pet. 35–39; Prelim. Resp. 15–29. For the reasons stated, we find that the present record, including Dr. Simpson's testimony, the FFT analysis he conducted on Huang2's image, and the

teachings of Ayres 2006 and Ayres 2008, supports Petitioner's contention that the claimed FFT analysis result with major adjacent peaks about 180° apart will be an inherent property of the aligned (anisotropic) collagen fibers taught by Huang2.

Claim 1 further recites "applying the scaffold to the tissue defect to repair a tendon, a ligament, or a nerve defect." Ex. 1001, cl. 1. Petitioner acknowledges that Huang2 does not disclose repairing a tendon, a ligament, or a nerve defect using the scaffolds described therein. Thus, Petitioner turns to the teachings of Kuo, which discloses a method for "replacing or enhancing a tissue" that comprises "(a) forming a tissue construct by contacting a scaffold sheet of fibrous material with a cell; and rolling the scaffold sheet in a jelly-roll like manner to form a spirally wound tissue construct, (b) implanting the spirally wound tissue construct into a subject in need of tissue replacement or regeneration, wherein the spirally wound tissue construct replaces a tissue." Pet. 39 (citing Ex. 1018, [0022]).

Petitioner further points to Kuo's teaching that the tissue to be replaced or regenerated is "selected from the group consisting of a muscle, a nerve, a ligament, a tendon, or another tissue." *Id.* (citing Ex. 1018, [0023]).

Petitioner contends that a POISITA "would have been motivated to use Huang2's aligned fibers, as shown by FFT analysis, which mimic the structure of the natural tendon, ligament, or nerve, and are stated to improve cell growth, to fabricate a scaffold to treat a tendon, ligament, or a nerve defect as taught by Kuo." *Id.* at 39–40 (citing Ex. 1003 ¶ 131). Petitioner contends the motivation would be based on the desirability of using aligned fibers to mimic native tissues such as tendon, ligaments, and nerves. *Id.* at 40 (citing Ex. 1003 ¶¶ 133–35; Ex. 1018, [0006], [0112]). Petitioner further contends that there would be a reasonable expectation of success given that

both Huang2 and Kuo successfully created scaffold of aligned fibers comprising collagen. *Id.* at 40–41 (citing Ex. 1003, § A.1.d).

Patent Owner argues that Petitioner does not identify a sufficient reason to combine Huang2 and Kuo to treat the specific types of tissue defects identified in claim 1. Prelim. Resp. 32–40. In particular, Patent Owner contends that Petitioner’s assertion that Huang2 and Kuo “are in the same field of art, and both seek to solve the same problems” is legally insufficient. *Id.* at 32–34. Patent Owner further contends that Huang’s scaffolds are only used for skin repair while Kuo’s scaffolds used for tendon and ligament repair involve a unique rolled structure not present in Huang2. Prelim. Resp. 34–39.

At this stage, we find some merit to Patent Owner’s argument the scaffolds in Huang2 and Kuo are directed to different types of tissue repair, and that Kuo specifically discusses a scaffold with a rolled structure not present in the scaffold taught by Huang2. We have considered Dr. Simpson’s opinion that the motivation to use Huang2’s aligned fibers would come from the knowledge that tendon, ligament, and nerve tissues are naturally aligned, and thus a POSITA would want to use a scaffold that mimics the natural alignment. Ex. ¶¶ 133–35. We note, however, that Kuo already discloses aligned fibers but further discloses the rolled structure to mimic the fascicles of muscle, tendon, nerve, or ligament tissue. Ex. 1018, [0034]. It is not clear why a POSITA would have chosen to use Huang2’s scaffold in place of the scaffolds taught by Kuo for the repair of tendon, nerve, or ligament tissue when Huang2 does not teach the same rolled structure that mimics the natural tendon, nerve, or ligament tissue. Petitioner does not address Kuo’s teaching regarding this rolled structure at all, let alone present any rationale to modify Huang2’s scaffolds to mimic

this rolled structure of natural tendon, nerve, or ligament issue, or otherwise explain why a POSITA would not seek to mimic that rolled structure when developing a scaffold to repair those specific types of tissues. Nonetheless because we are instituting on all grounds, we will further evaluate the merits of this ground after a full record is developed at trial.

Patent Owner does not present any separate arguments for dependent claims 2–6. We find that Petitioner has sufficiently demonstrated that Kuo discloses the scaffold may be formed as a sheet, thereby satisfying the requirement of dependent claim 2 (requiring “one or more elongated sheets”) and dependent claim 3 (requiring “multiple layers of one or more sheets”). See Pet. 41–43; Ex. 1018, [0007], [0020], [0022]. However, with regard to dependent claim 4 (reciting that “the tissue defect is a [] nerve defect”), dependent claim 5 (reciting that “the tissue defect is a [] ligament defect”), and dependent claim 6 (reciting that “the tissue defect is a [] tendon defect”), we share the same concerns discussed above as to whether a POSITA would have motivated to use Huang2’s scaffold to treat those specific types of tissue defects.

G. Analysis of Grounds 2: Obviousness of Claims 1–6 Based on Lee Alone, or Lee Combined with Kuo

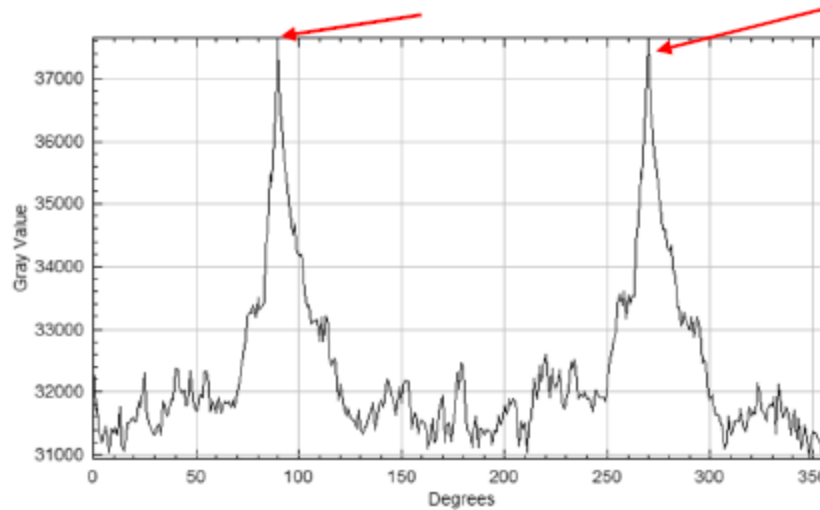
In Ground 2, Petitioner further contends that claims 1–6 would have been obvious based on the teachings of either Lee alone or the combination of Lee and Kuo. Although we have already made a determination to institute an *inter partes* review on all grounds set forth in the Petition, we provide some guidance to the parties with regard to this ground below. We once again focus our discussion of this ground on the issues raised with regard to independent claim 1.

With regard to the claim requirement for treating a tissue defect by implanting a scaffold, Petitioner points to Lee's teaching of an aligned scaffold used for skeletal muscle regeneration. Pet. 46 (citing Ex. 1011, [0005]–[0006], [0028]). With regard to the requirement that the scaffold comprise crosslinked collagen fibers, Petitioner points to Lee's teaching of “crosslinking said fibers to form the scaffold,” and that “electrospun PCL/collagen nanofiber meshes were cross linked under vapor of 2.5% glutaraldehyde solution for 6 hr to increase stability and strength of collagen.” *Id.* at 47 (citing Ex. 1011, [0005]–[0006], [0063]). Patent Owner does not dispute that these elements are taught by Lee. We agree with Petitioner that these claim elements are disclosed by Lee.

With regard to requirement that the fibers exhibit an FFT analysis result having “major adjacent peaks that are 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. 47–50. In particular, Lee discloses that “fiber orientations were induced by electrospinning onto a collector at different rotation rates.” Ex. 1011, [0061]. 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. 48–49. Petitioner contends that the image analysis from these figures in the provisional application show that Lee discloses highly aligned fibers. *Id.* at 49.

With respect to these grounds, Petitioner does not clearly assert in the Petition that the fibers taught by Lee necessarily or inherently satisfy the claimed FFT analysis result. 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).

Although Petitioner does not clearly assert that Lee's fibers inherently satisfy the FFT requirement, Petitioner contends that a POSITA “would know that the degree of alignment could also be determined using ImageJ software to run an ‘FFT analysis.’” Pet. 50. 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. 50. 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 ¶¶ 183–84. 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.* ¶¶ 185–86 (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 grounds based on Huang2. Prelim. Resp. 41–49. Patent Owner argues that Lee does not disclose any FFT results, and the mere disclosure of fiber alignment is insufficient to satisfy this limitation. *Id.* at 41. 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 47. 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 47–48.

For the reasons already discussed above with regard to the challenges based on Huang2, we are not persuaded by Patent Owner's arguments at this stage of the proceeding. 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 likely 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.

With regard to the requirement specifying that the tissue defect is a tendon, ligament, or nerve defect, Petitioner acknowledges that Lee does not expressly disclose using the scaffolds to repair those specific types of tissue defects. Pet. 51–52. Nonetheless, Petitioner contends that this claim element would have been obvious in view of Lee alone because a POSITA would understand that a scaffold used to treat muscle injury could also be used to treat a tendon or ligament injury given the similarity of the tissues. *Id.* (citing Ex. 1003, §VI.B.1.d). Alternatively, Petitioner contends that the

repair of those specific tissue defects would have been obvious when Lee is viewed in combination with Kuo, which expressly teaches using an engineered scaffold comprising crosslinked aligned collagen fibers to repair multiple tissue injuries, including, tendon, ligament, and nerve. *Id.* at 52 (citing Ex. 1018, [0005], [0022-23], [0052], Ex. 1003, §VI.B.1.d). Petitioner asserts that the motivation would be based on the desirability of using aligned fibers to mimic native tissues such as muscles, tendons, ligaments, and nerves. *Id.* at 52–53 (citing Ex. 1003 ¶¶ 194–96; Ex. 1018, [0006], [0034], [0112], Ex. 1019, 27).

In response, Patent Owner argues that Lee does not disclose repairing any other types of tissues other than muscle, and that Lee’s use of aligned myotubes are specifically directed to muscle tissue repair. Prelim. Resp. 50–51. Patent Owner argues that Dr. Simpson’s testimony is conclusory and unsupported and should be afforded little or no weight under 37 C.F.R. § 42.65(a). *Id.* at 51–52. With regard to Petitioner’s reliance on Kuo’s teaching of using aligned scaffolds to repair muscles, tendons, ligaments, and nerves, Patent Owner argues that Kuo does not indicate that the same scaffold can be used to repair each type of tissue, but instead teaches that scaffolds are seeded with different cell types appropriate for the type of tissue to be repaired. *Id.* at 52, 54–56. Patent Owner argues that Dr. Simpson improperly focuses on what a POSITA *could have* done rather than the legally operative question of whether a POSITA *would have* been motivated to make the modification or combination with a reasonable expectation of success. *Id.* at 53. Patent Owner also argues that Kuo’s scaffold used for tendon and ligament repair involve a unique rolled structure that is not present in Lee. *Id.* at 57.

Based on the present record, we are persuaded that Petitioner is likely to prevail with regard to its contention that a POSITA would have found it obvious to combine the teachings of Lee and Kuo to specifically treat tendon, ligament, or nerve defects. Kuo specifically discloses that its scaffolds can be used to treat muscle injuries, which is also the focus of Lee. Given that these references teach at least one common tissue that can be treated with aligned scaffolds disclosed therein, we find the present record supports Petitioner's contentions that a POSITA would also be motivated to utilize the aligned scaffolds taught in Lee to treat the other types of tissues identified in Kuo. We recognize there may be some differences in the specific structures of the scaffolds, such as the rolled structure disclosed in Kuo that is not disclosed in Lee. Nonetheless, because we are instituting as to all grounds presented in the Petition, we will further evaluate this issue after a full record is developed at trial.

III. CONCLUSION

For the forgoing reasons, Petitioner has demonstrated a reasonable likelihood that at least one challenged claim of the '227 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 '227 patent shall commence on

IPR2025-00249

Patent 11,318,227 B2

the entry date of this Order, and notice is hereby given of the institution of a trial.

IPR2025-00249
Patent 11,318,227 B2

FOR PETITIONER:

Howard Levine
Jennifer Swan
HOGAN LOVELLS US LLP
howard.levine@hoganlovells.com
jennifer.swan@hoganlovells.com

FOR PATENT OWNER:

George Davis
Tyler VanHoutan
MCGURIEWOODS LLP
gdavis@mcguirewoods.com
tvanhoutan@mcguirewoods.com