

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

U.S. ENDOSCOPY GROUP, INC. (PETITIONER)

Petitioner

v.

CDX DIAGNOSTICS INC. (PATENT OWNER)

CASE IPR2014-00642

Patent 6,258,044 B1

CDX DIAGNOSTICS INC.'S NOTICE OF APPEAL

Pursuant to 35 U.S.C. §§ 141(c) and 142 and in accordance with 37 C.F.R. § 90.3, Patent Owner CDx Diagnostics Inc. (“CDx”) hereby appeals to the United States Court of Appeals for the Federal Circuit from the Final Written Decision of the Patent Trial and Appeal Board (“Board”) entered on Oct. 15, 2015 (Paper 25, a copy of which is attached as exhibit A), and from all adverse underlying orders, decisions, rulings, and opinions.

For the limited purpose of providing the Director with the information requested in 37 CFR §90.2(a)(3)(ii), CDx anticipates that the issues on appeal may include, but are not limited to, the following, as well as any underlying findings, determinations, rulings, decisions, opinions, or other related issues:

- Whether the Board’s decision that claims 1-8, 11-17, 23-28, 32, and 35-39 of the ’044 Patent are anticipated under 35 U.S.C. § 102(b) by Parasher (Exhibit 1003 – the Parasher reference) is correct;

- Whether the Board’s decision that claims 9, 10, 19, and 20 are obvious under 35 U.S.C. § 103(a) in view of the Parasher reference and Markus (Exhibit 1005 – the Markus reference) is correct; and

- Whether the Board erred in characterizing certain of CDx’s argument as “new” and therefore erred in refusing to consider those arguments in the Final Written Decision.

Simultaneous with this filing and in accordance with 37 CFR 90.2(a)(1), this Notice of Appeal is filed with the Director of the United States Patent and Trademark Office; filed with Board; and served upon the Petitioner in accordance with 37 C.F.R. §42.6(e). In addition, a copy of this Notice of Appeal, along with the required fees, are being filed with the Clerk's Office for the United States Court of Appeals for the Federal Circuit.

Respectfully submitted,

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EXHIBIT A

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

U.S. ENDOSCOPY GROUP, INC.,
Petitioner,

v.

CDX DIAGNOSTICS, INC.,
Patent Owner.

Case IPR2014-00642
Patent 6,258,044 B1

Before PHILLIP J. KAUFFMAN, SCOTT A. DANIELS, and
BARRY L. GROSSMAN, *Administrative Patent Judges*.

DANIELS, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. BACKGROUND

A. *Procedural History*

Petitioner, U.S. Endoscopy Group, Inc., filed a Petition (Paper 4, “Pet.”) seeking *inter partes* review of claims 1–39 of U.S. Patent No. 6, 258,044 B1 (Ex. 1001, “the ’044 patent”).¹ Patent Owner, CDx Diagnostics, Inc., filed a Preliminary Response. Paper 6 (“Prelim. Resp.”).

In the Decision to Institute (Paper 7, “Inst. Dec.”), we instituted trial on claims 1–17, 19–20, 23–28, 32, and 35–39 based on the following grounds:

1) claims 1–8, 11–17, 23–28, 32, and 35–39 based under 35 U.S.C. § 102(b) by Parasher²; and

2) claims 9, 10, 19, and 20 under 35 U.S.C. § 103(a) over Parasher and Markus.³

Subsequently, Patent Owner filed a Patent Owner Response⁴ (Paper 14, “PO Resp.”), and Petitioner filed a Reply (Paper 16, “Pet. Reply”).

Patent Owner did not file a motion to amend. Neither party filed a motion to exclude evidence.

At the request of both parties, oral hearing was held on Thursday May 21, 2015. Papers 18, 20, and 21. A transcript of the oral hearing is included in the record. Paper 24 (“Tr.”).⁵

¹ We refer to the Corrected Petition, filed April 28, 2014.

² U.S. 5,535,756, issued July 16, 1996 (Ex. 1003).

³ U.S. 5,407,807, issued April 18, 1995 (Ex. 1005).

⁴ We refer to Patent Owner’s Corrected Patent Owner’s Response, filed February 9, 2015.

⁵ A single Transcript was created for the oral hearing for IPR2014-00639, IPR2014-00641, and IPR2015-00642. *See the Related Proceedings* section below.

For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–17, 19, 20, 23–28, 32, and 35–39 of the '044 patent are unpatentable.

B. Related Proceedings

Petitioner asserted the '044 patent in *CDx Diagnostics, Inc. v. U.S. Endoscopy Group, Inc.*, Case No. 1:13-cv-5669-NSR (S.D.N.Y.). Pet. 2.

The parties are also involved in IPR2014-00639, a challenge to U.S. 6,676,609 B1 (the "'609 patent") and IPR2014-00641 challenging U.S. Patent No. 7,004,913 B1 (the "'913 patent"). The '609 patent, the '913 patent, and the '044 patent all relate to similar subject matter of a brush for obtaining a patient biopsy. The '044 patent is, however, not related to the '609 patent or the '913 patent.

II. THE '044 PATENT

The '044 patent relates to a method and apparatus for obtaining cells from multiple layers of epithelium by abrasion and without laceration. Ex. 1001, 4:55–5:8; 5:25–28. In a preferred embodiment, the apparatus includes a brush having bristles of sufficient stiffness to allow them to dislodge and sweep up cells from superficial, intermediate, and basal layers of epithelium, and to penetrate the basement membrane underlying the epithelium to reach the submucosa, without having to resort to the dangers of incisional-based biopsy. *Id.* at 4:63–5:8; 5:24–40; 9:19–20. The brush is mounted on the distal end of a handle. *Id.* at 7:8–9. The bristles extend from wires that emanate from the distal end of the handle. The wires may form a toroid or spiral shape that is oriented substantially perpendicular to the axis of the handle. *Id.* at 7:23–28; Fig. 4. Figure 4 of the '044 patent is reproduced below:

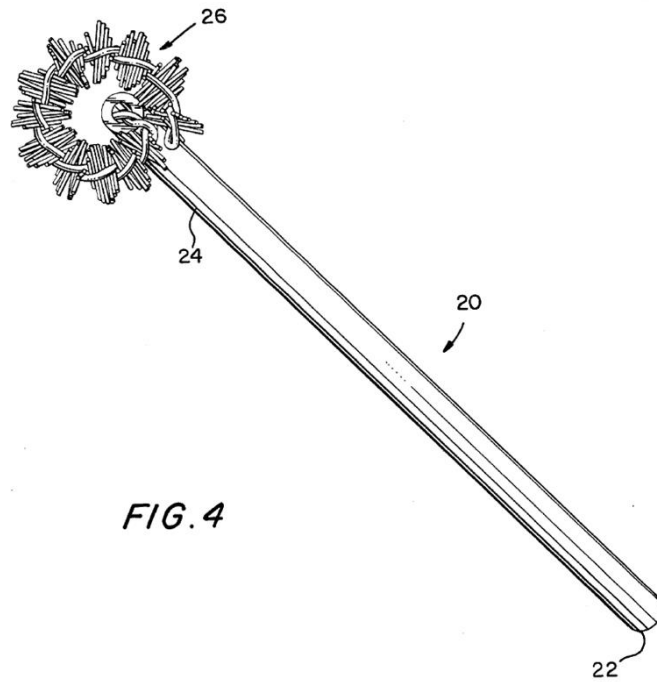
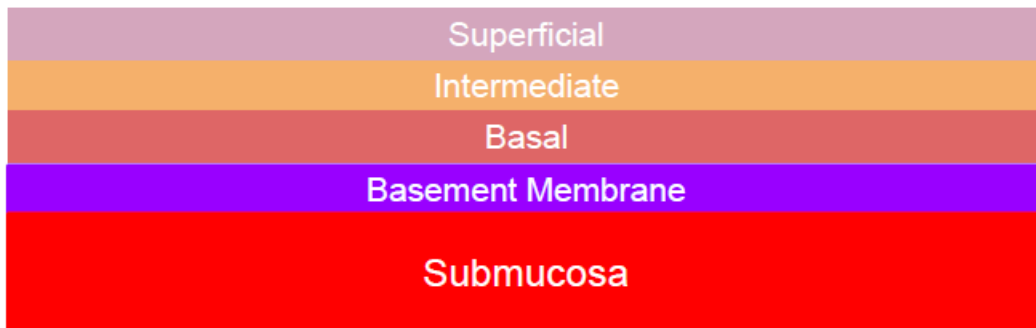


Figure 4 of the '044 patent illustrates a preferred embodiment shown in perspective view. *Id.* at 7:44–46.

Also helpful to our Decision, below, is an illustration of the layers of epithelial tissue. Epithelial tissue can be comprised of a superficial, intermediate, and basal layer, these three layers resting on the basement membrane which rests in turn on the submucosa. The figure on slide 4 of Patent Owner's demonstrative follows:



This figure depicts the layers of epithelial tissue adjacent to the basement membrane and submucosa. *See* Ex. 3002, 4⁶ (Patent Owner's demonstratives); Ex. 3003, 2 (Petitioner's demonstratives).⁷

The '044 patent describes its claimed apparatus through a contrast to cytology as well as lacerating biopsy. Cytology uses a soft brush to gently remove (sweep) previously freed cells (exfoliated or sloughed off) from the surface of the epithelium in a non-invasive manner that avoids or minimizes abrasion of the epithelium and is intended to be painless. Ex. 1001 at 2:26–4:24. On the other hand, a lacerating biopsy uses a cutting instrument such as a scalpel or a laser to remove tissue for evaluation. *Id.* at 1:65–2:3. The described brush uses a stiffer brush and rubs harder than cytology so that the surface of the epithelium is penetrated. *Id.* at 4:63–5:2. In other words, the stiff brush penetrates the surface of the epithelium by dislodging cells (as opposed to sweeping up previously freed cells) and picks up those cells without the invasive effects and discomfort of lacerating biopsy. *Id.*

III. THE CHALLENGED CLAIMS

Independent claims 1, 12, and 26 are illustrative of the claimed subject matter and are reproduced below.

⁶ Citing Ex. 1001 at 4:34–37, 11:56–65.

⁷ We exercise our discretion and enter the parties' demonstratives, which we earlier ordered to be served and not filed. *See* Paper 21, 2–3. This information appears uncontested in that the parties each depict the layers in the same manner. *Compare* Ex. 3002, 4, *with* Ex. 3003, 2. We discern no evidence in the case that contradicts this depiction.

1. Apparatus to obtain cells in epithelial tissue of the body comprising:

transepithelial non-lacerational sampling apparatus to collect cells from at least two layers of said epithelial tissue, said transepithelial non-lacerational sampling apparatus comprising a brush, said brush comprising bristles having sufficient stiffness to penetrate at least said two layers of said epithelial tissue.

12. A transepithelial non-lacerational sampling apparatus to harvest cells in an oral cavity from the epithelial tissue, said epithelial tissue comprising superficial, intermediate and basal layers, and a basement membrane located between the basal layer and the submucosa, said non-lacerational sampling apparatus comprising means to traverse said superficial, intermediate and basal layers and to collect cells from said three layers.

26. A method to collect cells in epithelial tissue of the body comprising:

passing a transipithelial⁸ non-lacerational sampling means through the epithelial tissue to collect cells from at least two layers of said epithelial tissue.

We determined in our Decision to Institute that no claim terms needed construction and that neither the term “means to traverse” in claim 12, nor “sampling means” in claim 26, invoked 35 U.S.C. § 112, sixth paragraph. Inst. Dec. 5, 7–8. Neither party disputed this determination nor offered further constructions of any claim terms or words. *See* PO Resp. 1, Reply 1–2. We

⁸ For purposes of this Decision, we understand the term “transipithelial” as “transepithelial.” The error appears to have been introduced by the Office. *Compare* Ex. 1001, 11:50, *with id.* at 13:28.

expressly interpret only those claim terms that require analysis to resolve arguments related to the patentability of the contested claims. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (only those terms which are in controversy need to be construed, and only to the extent necessary to resolve the controversy). All claim terms not explicitly construed are given the plain and ordinary meaning that the term would have had to a person of ordinary skill in the art, without further elaboration. 37 C.F.R. § 42.100(b). Because no part of our Decision relies on any specific construction of any claim term, no claim construction is necessary and the claims are accorded their broadest reasonable interpretation consistent with the specification of the '044 patent, reading claim language in light of the specification as it would be interpreted by one of ordinary skill in the art. *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004).

IV. EVIDENTIARY ISSUES⁹

A. *Parasher Article (Ex. 1004)*

As evidence that the device disclosed in Parasher (Ex. 1004, “the Parasher brush”) is inherently capable of collecting a tissue sample as claimed, Petitioner contends that the Parasher Article¹⁰ describes using the Parasher brush to obtain a biopsy sample of tissue located below the surface of the epithelium. Pet. 11. It is critical to Petitioner’s contention that the brush used in the experiments described in the Parasher Article is the Parasher brush.

⁹ This analysis is applicable to both grounds of unpatentability.

¹⁰ Parasher, et al., *Endoscopic Retrograde Wire-Guided Cytology of Malignant Biliary Structures Using a Novel Scraping Brush*, GASTROINTESTINAL ENDOSCOPY, Vol. 48, No. 3, 1998 (Ex. 1004).

Although the Parasher device and the Parasher Article are each attributed to Vinod K. Parasher, that does not demonstrate convincingly the brush used in the experiments is the Parasher brush. *See* Ex. 1003, 1; Ex. 1004, 1. The Petition asserts that the Parasher Article, “describes patient trials of the brush [the Parasher brush].” Pet. 11. This attorney argument is not supported by citation to evidence. *See In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974). (attorney’s arguments do not take the place of evidence) (citation omitted). The Petition does not identify, nor do we discern, an explicit disclosure that the brush used for the experiments described in the Parasher Article was the Parasher brush. *See* Pet. 11–12; Ex. 1004.

Petitioner asserts that the Parasher Article utilized a brush having semi-rigid and rough bristles made from a Velcro® pad. *Id.* (citing Ex. 1004, 290–291).¹¹ Although the Parasher Article arguably discloses this information (Ex. 1004, 290), Petitioner does not explain how this information demonstrates that the brush used in the experiments described in the Parasher Article is the Parasher brush. For example, the Petition does not explain the relevance of this information by pointing out that the Parasher brush includes a Velcro® pad, nor does the Petition cite to such disclosure in Parasher. We recognize that a preferred embodiment of the Parasher brush includes bristles comprised of a Velcro® pad. *See e.g.* Ex. 1003, Abstract, 1:15. We also recognize that there are other similarities between the Parasher brush and the brush described in the Parasher Article. For example, both brushes are described as having mushroom-shaped bristles. *See* Ex. 1003, 2:51–57; Ex. 1004, 1. However, it is Petitioner’s burden to set forth the relevance of evidence to the challenge raised, including identifying specific portions of the evidence that support the challenge, and the Board may give no weight where a

¹¹ Exhibit 1004 does not contain a page 291.

petitioner has failed to identify specific portions of the evidence that support the challenge. 37 C.F.R. § 42.104(b)(5). Petitioner does not explain sufficiently the relevance of the Parasher Article, nor identify specific portions of the evidence (the Parasher Article and Parasher) to demonstrate persuasively that the brush described in the Parasher Article is the Parasher brush.

During the course of this proceeding, Patent Owner pointed out that Petitioner did not establish adequately that the Parasher Article describes use of the Parasher brush. PO Resp. 11–12. Petitioner responded with the contention that Patent Owner’s inherency arguments are not relevant, and that the Board did not reply upon inherency in the institution decision. *See* Pet. Reply. 12. Petitioner’s contentions are inapposite to Patent Owner’s argument. Petitioner’s Reply was a second opportunity to establish adequately that the experiments of the Parasher Article utilized the Parasher brush. Petitioner did not utilize that opportunity effectively.

According, we give no weight to the Parasher Article in our analysis.

B. Dr. Michel Kahaleh

Dr. Michel Kahaleh, Petitioner’s witness, provided a Declaration (Ex. 1011) and was deposed by Patent Owner (Ex. 2005). Dr. Kahaleh is a medical doctor and professor. Ex. 1011 ¶ 5.

1. Composition of a Biopsy Specimen

In support of the contention that Parasher’s brush is capable of collecting a specimen that includes cells from tissue located below the surface of the epithelium, Petitioner stated, “[o]ne of ordinary skill in the art would understand that a biopsy sample necessarily includes fragments of the epithelial tissue, as well as portions of the basement membrane and submucosa below the epithelium.” Pet.

9–10 (citing Exhibit 1011 ¶ 10). That is, Petitioner asserts that if a specimen is a “biopsy,” it necessarily includes cells from epithelial tissue, the basement membrane, and submucosa.

We are not persuaded by this evidence for several reasons. First, at deposition, Dr. Kahaleh consistently referred to a sample taken using a brush as a “brushing,” and a sample taken using a biopsy forceps as a “biopsy.” *See e.g.*, Ex. 2005, 15–17.¹² This suggests that the definition of a biopsy specimen in paragraph 10 of Dr. Kahaleh’s Declaration was not referring to a specimen collected with a brush. Indeed, Dr. Kahaleh confirmed during his deposition that paragraph 10 of his Declaration was referring to a biopsy specimen obtained via a forceps biopsy procedure. PO Resp. 6; Ex. 2005, 16; *see also* Ex. 1011 ¶ 6 (Parasher not listed as a document reviewed in preparation for the Declaration). For these reasons, paragraph 10 of Dr. Kahaleh’s Declaration adds nothing to Petitioner’s contention that Parasher’s brush is capable of collecting a specimen that includes cells from tissue located below the surface of the epithelium.

Petitioner asserts that paragraph 16 of Dr. Kahaleh’s Declaration supports the contention that a brush biopsy specimen includes “tissue located below the top surface of the epithelium including basement membrane and submucosa” as required by claim 1. Pet. Reply 5 (quoting Ex. 1011 ¶ 16). As explained above, Dr. Kahaleh did not review Parasher before making this statement. *See* PO Resp. 10–11; Ex. 2005, 6:18–7:6.¹³ Therefore, at most, Dr. Kahaleh’s statement conveys that some unspecified brush is capable of obtaining such a specimen. The question

¹² When asked “so that when you use the brush you’re really not doing a biopsy, is that your opinion?” Dr. Kahaleh responded “right.” Ex. 2005, 17.

¹³ Further supporting this conclusion, Petitioner objected to Patent Owner’s question as beyond the scope of direct, suggesting that Dr. Kahaleh’s Declaration did not address the Parasher reference. *See* Ex. 2005, 6:25–7:3.

before us is not whether some brush has the claimed capability; the question is whether Parasher's brush has such capability. The proffered evidence sheds little or no light on the capabilities of Parasher's brush.

Petitioner contends that Dr. Kahaleh testified that "brushing" (use of a brush to obtain a specimen for examination) can obtain a specimen as claimed. Pet. Reply 4 (citing Ex. 2005, 17–18, 27–28). In the cited portions, Dr. Kahaleh testified with regard to the capabilities of the U.S. Endoscopy brush ("biliary brush") and not with regard to Parasher's brush. Therefore, this evidence sheds little or no light on the capabilities of Parasher's brush.

For these reasons, we determine that paragraphs 10 and 16 of Dr. Kahaleh's Declaration (Ex. 1011) and the portions of Dr. Kahaleh's testimony relied upon as detailed above, to be unpersuasive regarding the capability of Parasher's brush to gather a specimen as claimed.¹⁴

2. *Dr. Kahaleh's Qualifications*

Patent Owner makes two arguments why we should give the testimony of Dr. Kahaleh little or no weight. First, Patent Owner contends that Dr. Kahaleh is not an expert to testify as to what constitutes a biopsy, analyzing biopsy specimens, diagnosing disease based on review of biopsy specimens, and making determinations as to the sufficiency and/or adequacy of biopsy specimens. PO Resp. 22 (citing Ex. 2005, Tr. 30). According to Patent Owner, the relevant expert would be a pathologist or someone with similar knowledge of biopsies. PO Resp. 22–23. For these reasons, Patent Owner contends that we should give Dr. Kahaleh's testimony little or no weight. *Id.* at 25.

¹⁴ Because we do not rely upon Dr. Kahaleh's definition of biopsy, we need not address Patent Owner's argument that to do so is improper gap filling. *See* PO Resp. 21.

As an initial matter, we note that Patent Owner is not seeking to exclude Dr. Kahaleh's testimony, and therefore we need not consider whether Dr. Kahaleh is qualified as an expert under the Federal Rules of Evidence ("Fed. R. Evid."). *See* 37 C.F.R. §§ 42.62, 42.64; Fed. R. Evid. 702.

We disagree with Patent Owner's assertion that the relevant expert is limited to a pathologist.¹⁵ The field of the '044 patent relates to *obtaining* transepithelial specimens, not the study of the specimens so obtained. *See* Ex. 1001, 1:10–12. Indeed, all of the claims of the '044 patent deal with obtaining a specimen with a brush, and none of the claims deal with examination of that specimen. Therefore, expertise in the obtaining of specimens with a brush has relevance to the claimed subject matter.

Dr. Kahaleh has a medical science degree (cum laude) as well as a doctor of medicine. Ex. 1011 ¶ 2 (referring to Exhibit A attached thereto). He completed an internship in surgery, two fellowships in gastroenterology,¹⁶ and an internship and residency in internal medicine. *Id.* He is skilled in the art and use of endoscopic tools, including brushes for use in gastroenterology. *Id.* ¶ 4. For example, he has served as a Chief of Endoscopy and a Chief of Advanced Endoscopy, is board certified in internal medicine and gastroenterology, and has performed between 3,000 and 5,000 brush procedures for obtaining cells from multiple layers of epithelium. Ex. 2005, 27. From this and other information provided regarding Dr.

¹⁵ "Pathologist: [a] specialist in diagnosing the morbid changes in tissues removed at operations and postmortem examinations," *TABER'S CYCLOPEDIA MEDICAL DICTIONARY* (F.A. Davis Company, 12th ed. 1973), Ex. 3003, 3.

¹⁶ "Gastroenterology: [t]he branch of medical science concerned with study of physiology and pathology of the stomach, intestines, and related structures such as the esophagus, liver, gallbladder, and pancreas." *TABER'S CYCLOPEDIA MEDICAL DICTIONARY* (F.A. Davis Company, 12th Ed. 1973), Ex. 3003, 4.

Kahaleh, we determine that Dr. Kalahel has experience relevant to the field of the invention, and Patent Owner's argument that we should give such testimony little or no weight is not persuasive.

Second, Patent Owner contends that we should give Dr. Kahaleh's testimony little or no weight because, "Dr. Kahaleh did not 'have the skill and experience of an ordinary worker in the field,' and he did not 'have knowledge of all pertinent prior art' in May of 2001." PO Resp. 24 (citing *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962–63 (Fed. Cir. 1986); *Schott Gemtron Corp. v. SSW Holding Co.*, Case IPR2013-00358, slip op. at 18 (PTAB Aug 20, 2014) (Paper 106)).

The cited portion of *Custom Accessories* explains that when analyzing the level of skill in the art in a *Graham* analysis, the critical question is whether the claimed invention would have been obvious at the time to a person of ordinary skill in the art, who is a hypothetical person presumed to be aware of all the pertinent prior art. *Custom Accessories*, 807 F.2d at 962 (referring to *Graham v. John Deere Co.*, 383 U.S. 1 (1966)). *Custom Accessories* does not address whether an expert must have been qualified as of the critical date of the patent being discussed. *Id.*

Schott, a non-precedential Board decision, does not stand for the proposition that an expert witness must have been a person of ordinary skill in the art at the time of the claimed invention of the patent challenged. The Board did not cite to any legal authority with regard to being a person of ordinary skill as of the critical date. Rather, in context, the Board determined that Petitioner's witness was not a person of ordinary skill in the art at any time, to include at the time of the invention of the challenged patent. *Schott* at 18–19. A witness must provide testimony about the level of skill in the art as of the critical date; however, the witness need

not have acquired that knowledge as of the critical date. We note that in *Schott*, where the witness was not a person of ordinary skill in the art, the Board reduced the weight given that testimony and did not elect to give the testimony no weight.

Accordingly, Patent Owner's second argument that we should give Dr. Kahaleh's testimony little or no weight is not persuasive.

V. ANTICIPATION BY PARASHER

"Because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. § 102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements arranged as in the claim." *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (internal quotation marks omitted). Accordingly, an anticipatory reference must show all of the limitations of the claims "arranged or combined in the same way as recited in the claims." *Id.* at 1370; *see Finisar Corp. v. DirectTV Grp., Inc.*, 523 F.3d 1323, 1334–37 (Fed. Cir. 2008); *Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361 (Fed. Cir. 2000).

To prevail in its challenges to the patentability of claims, the petitioner must establish facts supporting its challenges by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

The burden of showing something by a preponderance of the evidence . . . simply requires the trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence.

Metro. Stevedore Co. v. Rambo, 521 U.S. 121, 137 n.9 (1997) (quoting *Concrete Pipe & Prods. of Cal., Inc. v. Constr. Laborers Pension Tr. for S. Cal.*, 508 U.S. 602, 622 (1993)).

Petitioner contends that claims 1–8, 11–17, 23–28, 32, and 35–39 are unpatentable as anticipated by Parasher. Pet. 7–21. We have considered the arguments and evidence presented by both parties, and we determine that Petitioner has shown by a preponderance of the evidence that claims 1–8, 11–17, 23–28, 32, and 35–39 are unpatentable as anticipated by Parasher.

A. Uncontested Aspects

Parasher discloses an apparatus, specifically a brush, to collect tissue cells located within epithelium tissue. Pet. 8; Ex. 1003, 1:8–11; 2:20–40; 3:6–32; 5:58–6:20; *see also* Ex. 1001, 1:16–19.

Figure 1 of Parasher follows:

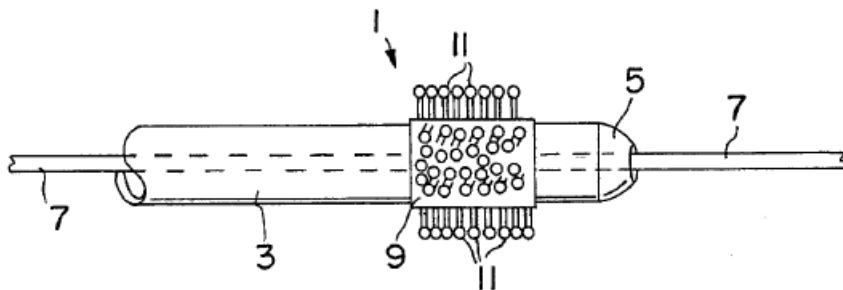


FIG. 1

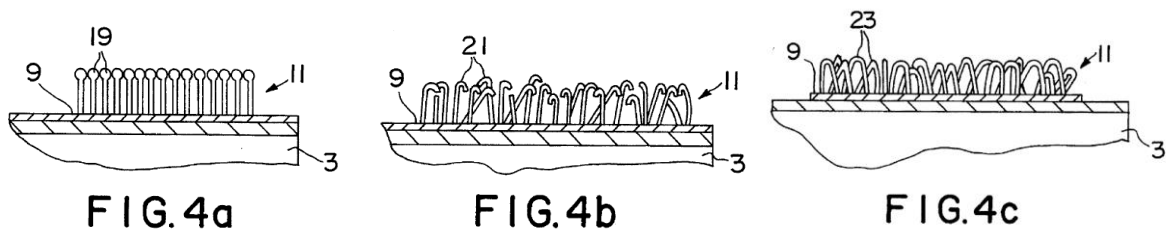
Figure 1 is a partial elevation view of a first embodiment of Parasher's apparatus. Ex. 1003, 4:7–8.

Parasher's device includes non-lacerational¹⁷ brush 9 having stiff or semi-rigid bristles 11. Pet. 8–9; Ex. 1003, 3:7–32; 4:46–48; 5:33–45, 5:58–6:20; Figs. 1–3. Parasher's brush is movable to bear against the tissue being examined and is

¹⁷ Parasher's brush reduces the risk of perforating the duct, suggesting the brush is non-lacerational. *See* Pet. 9–10, Ex. 1003, 2:16–19; *see also* Ex. 1003, 3:60–67 (Parasher's brushing procedure is safer than surgical extraction); Ex. 1013, 84 (Patent Owner's witness, Dr. Fromowitz, acknowledging that Parasher's brush is non-lacerational).

controlled to remove tissue from a tissue area being examined. Ex. 1003, 6:6–10. Specifically, Parasher’s brush is pushed and pulled back and forth over the inner wall of the duct to collect scrapings of tissue and brushings of cells. See Ex. 1003, 3:21–28; 6:6–10. Parasher describes this process as a “scrape biopsy.” Ex. 1003, 1:10–11; *see also* Ex. 1003, 1:14–17 (describing abrading against the duct walls); *Cf.* Ex. 1001, 6:35–37, 44–47 (describing the brush as moved or rubbed against the tissue to collect a specimen).

Parasher’s brush 9 is comprised of bristles 11 that are stiff or semi-rigid. Pet. 21; Ex. 1003, 4:46–58. As shown in Parasher’s Figures 4a–c, below, the tips of bristles 11 have features that facilitate collection of cell and tissue, such as hook ends, ball-tips, mushroom tips, loops, or the like. Pet. 8–9; Ex. 1003, 4:46–58; Figs 4a–4c; *Cf.* Ex. 1001, 7:15–20 (like the brush of the claim 1, the stiffness and shape of the bristle tips of Parasher contribute to the effectiveness of retrieving a specimen).



Figures 4a–c illustrate different embodiments of the bristles 11.

These contentions are not contested by Patent Owner. See 37 C.F.R. § 42.23(a) (any material fact not specifically denied may be considered admitted).

*B. Contested Aspect*¹⁸

Patent Owner contends that all of the claimed elements are not found within the four corners of Parasher, as is required for anticipation, because Parasher is silent regarding obtaining a specimen that includes tissue from below the surface of the epithelium. PO Resp. 3–4. Patent Owner sets forth several reasons why Dr. Kahaleh’s definition of biopsy proffered by Petitioner does not cure this deficiency. *Id.* at 5–10. Patent Owner’s arguments are, however, unpersuasive because Patent Owner mischaracterizes what is required for anticipation and does not address persuasively the merits of Petitioner’s contentions regarding Parasher.

1. Parasher

Patent Owner contends that Parasher is silent regarding the ability of the brush to penetrate and collect tissue from at least two layers of epithelial tissue. PO Resp. 3–5. We disagree both with the implication that Parasher must disclose such capability in the words of the ’044 patent and with Patent Owner’s characterization of the reference.

Parasher need not explicitly state that the device picks up tissue from multiple layers of the epithelium. *See generally In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990) (“These elements must be arranged as in the claim under review, but this is not an *ipsissimis verbis* test”) (citation omitted); *In re Gleave*, 530 F.3d 1331, 1334 (Fed. Cir. 2009) (although a reference must disclose each and every limitation in a claim to anticipate the claim, the reference need not satisfy an *ipsissimis verbis* test).

¹⁸ Our analysis does not address new arguments by Patent Owner meaning those arguments not in the record prior to oral hearing. *See* OFFICE PATENT TRIAL PRACTICE GUIDE, 77 Fed. Reg. 48,756, 48,768 (Aug. 14, 2012); Paper 23 (Petitioner’s objections to Patent Owner’s demonstratives).

The proper inquiry is what a person of ordinary skill in the art would understand as the capability of Parasher's brush. Further, contrary to Patent Owner's characterization, Parasher is not silent regarding the capabilities of the brush. Instead, as detailed below, Petitioner identifies and explains numerous disclosures regarding the extent of the specimen that is collected by Parasher's brush.

As detailed above, Parasher's device includes a brush having stiff or semi-rigid bristles with tips that facilitate the collection of cell and tissue. Further, Parasher's device obtains a specimen by bearing against the tissue being examined. Regarding the composition or extent of the specimen collected, Parasher's brush is capable both of collecting cells (cytology) and of collecting a larger (greater) sample of tissue (biopsy). Pet. 11; Pet. Reply 9; Ex. 1003, 1:8–11, 2:20–40, 3:26–28; *see also* Ex. 1003, Title (“Catheter with Simultaneous Brush Cytology and Scrape Biopsy Capability”); 3:60–67 (describing the sample collected as “more substantial” than that collected with conventional cytology). Parasher describes that the device enables collection of a “gross tissue sample” or biopsy. Pet. 11; Pet. Reply 7; Ex. 1003, 1:56–58; 2:20–25. Petitioner points out that Parasher also describes the brush as capable of collecting “a gross tissue sample that includes the mucous lining of the duct, the tissue of the duct, and even adjacent connective tissues (e.g., the submucosa).” Pet. 9 (citing Ex. 1003, 1:54–67); Pet. Reply 7–8.

A person of ordinary skill in the art would have considered these disclosures in the context that “tissue” is an aggregation of similarly specialized cells and that “gross” means large enough to be visible to the naked eye. *See* Ex. 2003, 4; 2004, 6; Ex. 3001,¹⁹ 5.

¹⁹ “Gross,” *TABER'S CYCLOPEDIA MEDICAL DICTIONARY*, 12th Ed., copyright 1973, F.A. Davis Company, Ex. 3001, 5

In light of this, Parasher's brush, like the claimed device, includes bristles that are stiff and have a shape that contributes to penetrating the tissue sample and collecting a specimen. Parasher's brush, like the claimed device, obtains a specimen by bearing against the tissue being examined. The specimen obtained by Parasher's brush is an aggregation of cells large enough to be visible to the naked eye. In light of the foregoing, we find that Petitioner has shown, by a preponderance of the evidence, that Parasher's brush obtains such a specimen by penetrating into the tissue being examined and, with sufficient force applied, penetrating through the tissue to the submucosa.

C. Dr. Fromowitz

Dr. Frank Fromowitz, Patent Owner's expert witness, provided a Declaration (Ex. 2001) and was deposed by Petitioner (Ex. 1013). Dr. Fromowitz is a licensed physician with 35 years of experience as a pathologist. Ex. 2001 ¶¶ 3, 4, 7. Each party relies upon the testimony of Dr. Fromowitz, and it is uncontested that Dr. Fromowitz is qualified to provide expert testimony. *See e.g.*, PO Resp. 26; Pet. Reply 1–2, 6–7.

1. Patent Owner

Patent Owner relies upon the testimony and Declaration of Dr. Fromowitz to attempt to counter Dr. Kahaleh's evidence regarding the composition of a biopsy specimen. PO Resp. 12. Because we are not considering Dr. Kahaleh's evidence regarding the composition of a biopsy specimen, Patent Owner's arguments are not relevant.

Patent Owner does not rely upon evidence from Dr. Fromowitz to attempt to counter Petitioner's analysis of Parasher. PO Resp. *passim*.

2. *Petitioner's Use of Dr. Fromowitz's Testimony*

Petitioner contends that Dr. Fromowitz “testified that the brush of Parasher collects the same sample of epithelial tissue, basement membrane and submucosa as claimed in the ‘044 Patent.” Pet. Reply 1 (citing Ex. 1013, 96). Our interpretation of this portion of Dr. Fromowitz’s testimony follows.

As background, Parasher discloses that, “[t]o diagnose a malignancy associated with a stricture, for example, it may be appropriate to examine the mucous lining of the duct, the tissue of the duct wall and *even adjacent tissues*.” Ex. 1003, 1:61–64 (emphasis added). Petitioner asked Dr. Fromowitz if “adjacent tissue” in this context included submucosa. Ex. 1013, 94:8–95:12. Dr. Fromowitz stated that it could refer to a different organ, such as the liver or duodenum, but subsequently added that it “would have to include the submucosa.” *Id.*

Petitioner subsequently directed Dr. Fromowitz’s attention to the disclosure that Parasher’s device can obtain a larger tissue than may be obtained with cytology so that the sample obtained is a gross tissue sample or biopsy. Ex. 1013, 95:13–22 (referring to Ex. 1003, 2:20–25). Dr. Fromowitz interpreted this disclosure to state that a brush can be used to get more tissue than may be obtained by cytology, and that the sample obtained would be a biopsy. Ex. 1013, 94:8–96:12. Dr. Fromowitz disagrees with the reference in that obtaining more cells does not mean the constituents of a biopsy have been obtained. *Id.* at 96:5–12. This observation must be interpreted in the light that Dr. Fromowitz considers a biopsy specimen to be “a segment of intact tissue” as may be obtained by cutting, pulling, excising or the like (methods other than brushing). *Id.* at 21:18–19. Therefore, Dr. Fromowitz is stating that he thinks a brush cannot obtain a segment of intact tissue. None of the challenged claims require the specimen to be a segment of intact tissue. Nor do the claims recite that the specimen obtained is a

“biopsy;” rather, the claims specify only “cells from at least two layers of said epithelial tissue” of the specimen obtained. *See e.g.*, Ex. 1001, claim 1 (requiring the specimen to include cells from at least two layers of the epithelium).

Petitioner contends that Dr. Fromowitz stated that the sample collected by Parasher is similar to a specimen as claimed and that Parasher’s brush “penetrates the layers of the epithelium and into the submucosa.” Pet. Reply 6 (citing Ex. 1013, 95:6–12, 96:13–18, 99:5–16, 99:24–100:4). Dr. Fromowitz did not explicitly state that the sample collected by Parasher is similar to a specimen as claimed. Ex. 1013, 96:13–18. Rather, in context, during his deposition Dr. Fromowitz testified that a “gross issue sample,” as used in Parasher, means a sample of tissue that you can actually see, and that it was “possible” that a scraping could include the submucosa. Ex. 1013, 95:16–96:18, 99:5–16 (referring to Ex. 1003, 2:20–25, 3:27). Subsequently, Petitioner then asked if scraping as disclosed by Parasher would obtain a specimen that included cells from the submucosa. *Id.* at 99:5–10. Dr. Fromowitz replied, “not necessarily,” and then added that Parasher’s device could obtain such a specimen, but not reliably so. *Id.* at 99:11–16.

Petitioner referred again to the disclosure that Parasher’s device can obtain a specimen that qualifies as a gross tissue sample or biopsy, and asked whether a person of ordinary skill in the art would understand this disclosure to mean that the specimen obtained includes portions of the submucosa. Ex. 1013, 99:20–100:4 (referring to Ex. 1003, 2:24–25). Dr. Fromowitz stated that in some instances it could. *Id.*

In light of this, we determine Dr. Fromowitz testified that Parasher’s device can obtain a gross tissue sample, meaning a sample that is visible to the naked eye, and this sample would include more cells than would be obtained by cytology. *See*

Ex. 1013, 95:16–96:18 (referring to Ex. 1003, 2:20–25); 94:8–96:12 (referring to Ex. 1003, 2:20–25). The size of the specimen collected (more cells than cytology and visible to the naked eye) supports Petitioner’s contention that Parasher’s device dislodges cells from not only the surface, but also from within the epithelium. This information is consistent with our analysis of Parasher above.

Further, Dr. Fromowitz testified three times that Parasher’s could obtain a specimen that included portions of the submucosa. Ex. 1013, 94:8–95:12 (referring to Ex. 1013, 1:61–64 and stating that a specimen “would have to include the submucosa”), 99:12–16 (referring to Ex. 1003, 3:26–28 and stating that Parasher’s device could obtain a specimen that included submucosa, but not reliably so), 99:20–100:4 (referring to Ex. 1003, 2:24–25 and stating that in some instances Parasher’s device could obtain such a specimen). This evidence is consistent with our analysis of Parasher above. This evidence suggests that Parasher’s brush not only is capable of dislodging cells from below the surface of the epithelium, but is also capable of penetrating to the submucosa.

D. Conclusions by Claim

1. Claim 1

Petitioner identifies and explains how Parasher discloses each element of claim 1, with the only contested aspect being whether Parasher’s brush is capable of collecting cells from at least two layers of the epithelium. Patent Owner challenges Dr. Kahaleh’s evidence regarding the composition of a biopsy; however, this challenge is not persuasive because our analysis of Petitioner’s case does not rely on this evidence. With regard to Petitioner’s analysis of Parasher, Patent Owner simply contends that Parasher is silent regarding the capabilities of the brush. To the contrary, Parasher is not silent, and Petitioner’s analysis of Parasher demonstrates that it is more likely than not that Parasher’s brush obtains

such a specimen by collecting cells from the various layers of the epithelium, including down to the submucosa. If a prior art structure is capable of performing the intended use, then it meets the claim. *See, e.g., In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997) (anticipation rejection affirmed based on Board’s factual finding that the reference dispenser (a spout disclosed as useful for purposes such as dispensing oil from an oil can) would be capable of dispensing popcorn in the manner set forth in appellant’s claim 1 (a dispensing top for dispensing popcorn in a specified manner)).

Dr. Fromowitz’s testimony is consistent with, and further supports Petitioner’s case.

We conclude that Petitioner has shown by a preponderance of the evidence that claim 1 is anticipated by Parasher.

2. *Claim 2*

Claim 2 depends from claim 1 and adds that the bristles of the brush collect cells from “three layers of . . . epithelial tissue, said three layers comprising superficial, intermediate and basal layers.” Parasher discloses that bristles 11 of brush 9 are sufficiently stiff to penetrate to the submucosa, thus penetrating the superficial, intermediate and basal layers of epithelium. Pet. 12; Ex. 1003, 2:41–46. Patent Owner repeats the arguments for claim 1, and these arguments are not persuasive for the reasons given above. PO Resp. 14.

We conclude that Petitioner has shown by a preponderance of the evidence that claim 2 is anticipated by Parasher.

3. *Claim 3*

Claim 3 depends from claim 2 and adds that the “bristles . . . have sufficient stiffness to penetrate said basement membrane and reach said submucosa.”

Parasher discloses that bristles 11 of brush 9 are sufficiently stiff to penetrate through the superficial, intermediate and basal layers to the submucosa. Pet. 12; Ex. 1003, 2:41–46. Patent Owner repeats the arguments for claim 1. PO Resp. 14. These arguments are unpersuasive for the reasons given above.

We conclude that Petitioner has shown by a preponderance of the evidence that claim 3 is unpatentable as anticipated by Parasher.

4. *Claims 4–8 and 11*

Claims 4–8 and 11 depend from claim 1. Patent Owner contends only that these claims are not anticipated by Parasher for the reasons explained with respect to claim 1. PO Resp. 17. These arguments are unpersuasive for the reasons given above. Further, these arguments do not address persuasively the additional limitations of claims 4–8 and 11. *See* 37 C.F.R. § 42.23(a).

5. *Claim 12*

Claim 12 is independent and specifies “a transepithelial non-lacerating sampling apparatus to harvest cells in an oral cavity from . . . epithelial tissue comprising superficial, intermediate and basal layers.” Patent Owner argues that Parasher “is silent as to a brush that ‘collects cells from three layers of . . . epithelial tissue,’ and which has a ‘means to traverse . . . superficial, intermediate and basal layers and to collect cells from said three layers’” as called for in claim 12. PO Resp. 17. We interpreted claim 12 including “means to traverse” as, among other things, encompassing a non-lacerational brush with stiff bristles as described in the ’044 patent. Inst. Dec. 8. Patent Owner’s arguments parallel those made with respect to claims 1 and 2, and are unpersuasive for the reasons set forth above.

6. *Claim 13*

Claim 13 depends from claim 12 and recites that the “means to traverse . . . comprises sufficient stiffness to traverse said basement membrane and reach into said submucosa.” Patent Owner asserts that Parasher does not disclose the brush “traversing the basement membrane and reaching the submucosa.” *Id.* at 18. For the reasons discussed above, we are also not persuaded by this argument.

7. *Claims 14–17 and 23–25*

Claims 14–17 depend indirectly from claim 1 and claims 23–25 depend directly from claim 12. Patent Owner contends only that these claims are not anticipated by Parasher for the reasons explained with respect to claims 1 and 12. *Id.* These arguments are unpersuasive for the reasons given above. Further, these arguments do not address persuasively the additional limitations of claims 14–17 and 23–25. *See* 37 C.F.R. § 42.23(a).

8. *Claims 26–28*

Claim 26 is an independent claim drawn to “[a] method to collect cells in epithelial tissue” including the step of “passing a transipithelial non-lacerational sampling means through the epithelial tissue to collect cells from at least two layers of said epithelial tissue.” Parasher discloses that “[t]he brush bearing end of the catheter is moved to the selected area of the duct and pushed and pulled, back and forth over the inner wall of the duct. The bristles of the brush collect sample scrapings of tissue and brushings of cells at the selected area.” Ex. 1003, 3:23–28. We determined for claim 26 that “transepithelial non-lacerational sampling means,” among other things, encompassed a stiff-bristled nonlacerational brush capable of penetrating epithelium, as disclosed in the ’044 patent. Inst. Dec. 9. For claim 26 Patent Owner repeats the arguments for claim 1. PO Resp. 18–19.

These arguments are unpersuasive for the reasons given above. With respect to claims 27 and 28, which depend from claim 26, Patent Owner argues that Parasher is silent regarding its non-lacerational brush penetrating three layers as well as the basement membrane. *Id.* at 19. As discussed above, we are not persuaded by these arguments.

9. *Claims 32 and 35–36*

Claims 32 and 35–36 depend from claim 26. Patent Owner contends only that these claims are not anticipated by Parasher for the reasons explained with respect to claim 26. *Id.* These arguments are unpersuasive for the reasons given above. Further, these arguments do not address persuasively the additional limitations of claims 14–17 and 23–25. *See* 37 C.F.R. § 42.23(a).

VI. OBVIOUSNESS OVER PRASHER AND MARKUS

Petitioner contends that claims 9, 10, 19 and 20 are unpatentable over Parasher (Ex. 1003) and Markus (Ex. 1005). Pet. 21–23. Specifically, Petitioner contends that Markus discloses a brush having bristles which fall within the stiffness range of 0.04 and 0.2 lbs/in as recited in claims 9 and 19, and also, within the range of 0.05–0.2 inches in length as recited in claims 10 and 20. *Id.* at 22–23. Petitioner argues that it would have been obvious to one of ordinary skill in the art to modify Parasher’s brush with Markus’s bristle characteristics as a simple substitution that obtains predictable results. *Id.* at 23.

Markus discloses culturing brush 10 having bristles 14 for collecting a sample of fibrin from a catheter inserted in a medical patient to facilitate determination of an infection. Ex. 1005, 1:60–68, 4:40–55. Bristles 14 are stiff or semi-rigid, made of Tynex® having a tangent modulus (E) of 500,000 psi, and are capable of exerting sufficient pressure to dislodge fibrin from the catheter. *Id.*

In the Preliminary Response, Patent Owner argued that Markus is not analogous to the claimed subject matter because it is not “a cell harvesting device.” Prelim. Resp. 11. In the Institution Decision we stated that “the evidence presently of record does not support Patent Owner’s contention that catheter brushes are non-analogous to cell harvesting devices.” Inst. Dec. 11. Patent Owner does not repeat these arguments in the Response, nor provide supporting evidence with respect to their analogous art contention for claims 9, 10, 19, and 20. *See* PO Resp. 17–18. Consequently our analysis has not changed.

Petitioner’s reasoning that modifying Parasher’s device to utilize bristles having the characteristics of Markus’s brush is a simple substitution with predictable results is persuasive in view of the fact that both Parasher’s and Markus’s brushes are used for medical sample collection are similar in size and shape and because Markus recognizes cytology brushes as within the prior art of its catheter brush.²⁰ *See* Pet. 21–22 (citing Ex. 1005, 4:40–55).

In the Response, Patent Owner relies on its argument that Parasher’s brush does not anticipate independent claims 1 and 12 from which claims 9, 10, and 19, 20 depend respectively. PO Resp. 17–18. Such argument is not responsive because Petitioner’s arguments supporting this ground of unpatentability rely upon Markus’s bristles, not Parasher’s. *See* Pet. 25–29.

At the oral hearing Patent Owner argued that Markus’s brush cannot be substituted into Parasher’s endoscope because Markus teaches not to damage the vein in which the catheter is inserted. *See* Tr. 77–79. Petitioner correctly objects

²⁰ The level of skill in the art is not explicitly set out by Petitioner, nor directly contested by Patent Owner. We consider the prior art of the ground of unpatentability to be representative. Secondary considerations are not contested in this case.

that this is a new argument. Paper 23, 3²¹; OFFICE PATENT TRIAL PRACTICE GUIDE, 77 Fed. Reg. 48,756, 48,768 (Aug. 14, 2012).²² Therefore, we do not consider this argument.

In light of this, Patent Owner has not challenged effectively any material fact in Petitioner's ground of unpatentability. *See* 37 C.F.R. § 42. 23(a).

Petitioner has demonstrated by a preponderance of the evidence that claims 9, 10, 19, and 20 are unpatentable over Parasher and Markus.

VII. CONCLUSION

Petitioner has met its burden of proof by a preponderance of the evidence that (1) claims 1–8, 11–17, 23–28, 32, and 35–39 are anticipated by Parasher and (2) claims 9, 10, 19, and 20 would have been obvious over Parasher and Markus.

VIII. ORDER

Accordingly, it is

ORDERED that claims 1–17, 19–20, 23–28, 32, and 35–39 of U.S. Patent 6,258,044 B1 are determined by a preponderance of the evidence to be unpatentable; and

FURTHER ORDERED that because this is a final written decision of the Board under 35 U.S.C. § 318(a), parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

²¹ The pages of this exhibit are not numbered.

²² *See also* Paper 21, 3 (directing the parties to *St. Jude Med., Cardiology Division, Inc. v. Board of Regents*, IPR2013-00041 (PTAB January 27, 2014) (Paper 65), for guidance regarding the appropriate content of demonstrative exhibits).

IPR2014-00642
Patent 6,258,044 B1

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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing Notice of Appeal was served electronically on this 12th day of November, 2015 to the persons listed at the addresses below:

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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing Notice of Appeal was electronically filed with the Board on this 12th day of November, 2015 and was delivered by hand delivery to the Director of the United States Patent and Trademark Office, at the following address:

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I hereby certify that a true and correct copy of the foregoing Notice of Appeal was served electronically on this 12th day of November, 2015 with the Clerk's Office of the United States Court of Appeals for the Federal Circuit, utilizing the Court's CM/ECF system, at the following address:

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