UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELEKTA INC.,
Petitioner

v.

BEST MEDICAL INTERNATIONAL, INC.,
Patent Owner.

Case No.: IPR2020-00073

U.S. Patent No. 7,266,175

PETITION FOR *INTER PARTES* REVIEW
OF U.S. PATENT NO. 7,266,175

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I. INTRODUCTION

Petitioner Elekta Inc. (Elekta) requests that the Board institute *inter partes* review (IPR) of and cancel claims 1, 8, 10-13, 17, 19, 20 ("Challenged Claims") of U.S. Patent No. 7,266,175 ('175 patent) (Ex. 1001), assigned to Best Medical International, Inc. ("BMI" or "Patent Owner"), in accordance with 35 U.S.C. §§311-319 and 37 C.F.R. § 42.100 *et seq*.

A. Declaration Evidence

This Petition is supported by declaration testimony of Dr. Joao Seco (Seco Declaration) (Ex. 1003), which incorporates by reference declaration testimony of Dr. Arthur Boyer ("Boyer SOA Declaration") (Ex. 1021), and declaration testimony of Marla Hirth (Ex. 1029). Boyer SOA Declaration. The Seco Declaration describes the '175 patent, the POSITA in the relevant time frame, interpretation of certain terms in the '175 patent, the state of the art of the '175 patent, the scope and content of the prior art compared to the claims of the '175 patent, and the rationales for combining prior art elements. The Boyer SOA Declaration describes the general state of the art in radiotherapy in the 1990s.

II. MANDATORY NOTICES UNDER 37 C.F.R. §42.8(A)(1)

A. Real Parties-in-Interest (37 C.F.R. § 42.8(b)(1))

Petitioner identifies Elekta Limited (UK), Elekta Holdings U.S., Inc. and Elekta AB as real parties in interest without admitting that they are in fact real parties in interest. Elekta Limited (UK), Elekta Holdings U.S., Inc. and Elekta AB have agreed to be bound by the estoppel provisions of 35 U.S.C. 315(e) to the same extent as Petitioners.

B. Related Matters (37 C.F.R. § 42.8(b)(2))

Patent Owner asserted the ’175 patent in *Best Medical International, Inc.* v. *Elekta, Inc. and Elekta, Limited*, Civil Action 1:19-cv-03409-MLB (currently pending in the Northern District of Georgia, and previously pending in the District of Delaware as Civil Action No. 1:18-cv-01600-MN) and *Best Medical International, Inc*. v. *Varian Medical Systems, Inc. et al*, Civil Action 1:18-cv-01599 (currently pending in the District of Delaware).

The ’175 patent is the subject of IPR 2020-00053 filed October 17, 2019. Case IPR 2020-00053 involves challenges to claims 13, 14, 15, 16, 18 and 19 of the ’175 patent based on Webb 2001, Mohan 2000, Webb 1993, and Siebers 2002. The Patent Owner has not yet filed preliminary responses in this proceeding. Case IPR 2020-00053 does not involve claim 1, 8, 10, 11, 12, 17 and 20 of the ’175 patent, which are at issue in this petition. In addition, primary references presented

in this Petition (including Shepard 2002, Que 1999, and Bar 2001) are new and not included in Case IPR 2020-00053. The arguments and evidence presented in this Petition are not the same or substantially the same as those presented to the Board in Case IPR 2020-00053. Moreover, this Petition is necessary to address at least claims 1, 8, 10, 11, 12, 17 and 20 in view of the prior art references cited in this Petition.

C. Counsel (37 C.F.R. § 42.8(b)(3)) and Service Information (37 C.F.R. § 42.8(b)(3)-(4))

Petitioner designates Tamara D. Fraizer (Reg. No. 51,699) as lead counsel for this matter. Petitioner designates Vid R. Bhakar (Reg. No. 42,323) and Christopher W. Adams (Reg. No. 62,550) as back-up counsel for this matter.

Postal mailings and hand-deliveries for lead and back-up counsel should be addressed to: Tamara D. Fraizer, Squire Patton Boggs (US) LLP, 1801 Page Mill Road, Suite 110, Palo Alto, CA 94304-1043 (Telephone: (650) 843-3201; Fax: (650) 843-8777).

Pursuant to 37 C.F.R. § 42.8(b)(4), Petitioner consents to e-mail service at: tamara.fraizer@squirepb.com; sfripdocket@squirepb.com.

For compliance with 37 C.F.R. § 42.10(b), a Power of Attorney is also filed concurrently herewith.

III. CERTIFICATION (37 C.F.R. § 42.104(A)) AND PAYMENT OF FEES (37 C.F.R. § 42.10)

Petitioner certifies that the ’175 patent is available for IPR and Petitioner and the real parties-in-interest are not barred or estopped from requesting IPR on the grounds identified herein.

The complaint referenced in Section II.B was served within the last 12 months. Neither the Petitioner nor its real parties-in-interest (or privies), have been served with any other complaint alleging infringement of the ’175 patent.

The undersigned authorizes the USPTO to charge any fees due during this proceeding to Deposit Account No. 07-1850.

IV. IDENTIFICATION OF CLAIMS AND GROUNDS (37 C.F.R. § 42.104(A), (B))

The application for the ’175 patent was filed on July 09, 2004 by Nomos Corporation, the Patent Owner’s predecessor-in-interest. This application claimed priority to U.S. Provisional Application No. 60/487,067, which was filed on July 11, 2003. Ex. 1003 ¶133.

Because the filing date of the ’175 patent (and all applications to which it claims priority) is before the effective date of the AIA (March 16, 2013), the pre-AIA statute applies.

For purposes of this IPR, Petitioner treats July 11, 2003 as the effective filing date of the cited provisional applications, as the “Alleged Priority Date” for

all Challenged Claims. To the extent that the Patent Owner demonstrates a date of conception earlier than this, then the Petitioner shall reserve the right to adjust the "Alleged Priority Date" accordingly.

Petitioner relies on the following references:

A. Non-Patent Literature

Whether a reference constitutes a printed publication under § 102(b) is a legal conclusion based on underlying factual determinations. *GoPro, Inc.* v. *Contour IP Holding LLC*, 898 F.3d 1170, 1173-74 (2018). The Federal Circuit has "interpreted §102 broadly, finding that even relatively obscure documents qualify as prior art so long as the relevant public has a means of accessing them." *Id.* 1174. A reference is "publicly accessible if it was disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it." *Id.*

Shepard 2002, Que 1999, Webb 2001, Siebers 2002, Bar 2001 are authentic copies of the references from their respective publications. Exs. 1010, 1012, 1005, 1008, 1014; Ex. 1029 Hirth Declaration. Except for Bar 2001, each of the other references has (i) either a date stamp from the National Library of Medicine or (ii) a copyright office stamp from the Library of Congress, Copyright office, each of which signify when such institution processed the article. *Id*. *SAP America, Inc.* v. *Realtime Data, LLC*, IPR2016-00783, 2016 WL 667819 (PTAB Oct. 5, 2016).

None of the following references below are listed on the face of the ’175 patent and therefore they were never disclosed to or considered by the Examiner during prosecution.

1. Shepard 2002 (Ex.1010)

Shepard 2002 is a printed publication bearing a copyright date of 2002 and first published by the American Association of Physicists in Medicine (AAPM) in International Journal of Medical Physics Research and Practice, Issue: 6, Volume: 29, Page: 1007-1018. Ex. 1010 1007 (“© 2002”); *LG Elec., Inc. v. Advanced Micro Devices, Inc.*, IPR2015-00329, Paper 13 12 (PTAB Jul. 10, 2015) (copyright date is prima facie evidence of publication). Ex. 1029 ¶¶69-76. Shepard 2002 is § 102(b) prior art because it was publically accessible a year before the Alleged Priority Date.

2. Que 1999 (Ex. 1012)

Que 1999 is a printed publication bearing a copyright date of 1999 and first published by AAPM in International Journal of Medical Physics Research and Practice, Issue: 11, Volume: 26, Page: 2390-2396. Ex. 1012 2390, (“© 1999); *LG Elec., Inc.* v. *Advanced Micro Devices, Inc.*, IPR2015-00329, Paper 13 12 (PTAB Jul. 10, 2015) (copyright date is prima facie evidence of publication). *See* Ex. 1029 ¶¶77-84. Que 1999 is § 102(b) prior art because it was publically accessible a year before the Alleged Priority Date.

3. Webb 2001 (Ex. 1006)

Webb 2001 is a printed publication bearing a copyright date of 2001 and first published by IOP Publishing Ltd. in the United Kingdom in "July 2001." Ex. 1006 cover page ("July 2001"), N187 ("© 2001"); *LG Elec., Inc.* v. *Advanced Micro Devices, Inc.*, IPR2015-00329, Paper 13 12 (PTAB Jul. 10, 2015) (copyright date is prima facie evidence of publication). Ex. 1029 ¶¶44-60. Webb 2001 is § 102(b) prior art because it was publically accessible a year before the Alleged Priority Date.

4. Siebers 2002 (Ex. 1008)

Siebers 2002 is a printed publication bearing a copyright date of 2002 and first published by AAPM in International Journal of Medical Physics Research and Practice, Issue: 6, Volume: 29, Page: 952-959. Ex. 1008 952, ("© 2002); *LG Elec., Inc.*, Paper 13 12 (copyright date is prima facie evidence of publication). Ex. 1029 ¶¶61-69. Siebers 2002 is § 102(b) prior art because it was publically accessible a year before the Alleged Priority Date.

5. Bar 2001(Ex. 1014)

Bar 2001 is a printed publication first published by IOP Publishing Ltd. in Physics in Medicine & Biology, Volume 46, Number 7. Ex. 1014 952. According

to the publisher's website, Volume 46, Number 7 was published in July 2001.[1] Ex. 1029 ¶¶85-90. Bar 2001 is § 102(b) prior art because it was publically accessible a year before the Alleged Priority Date.

V. TECHNOLOGY BACKGROUND

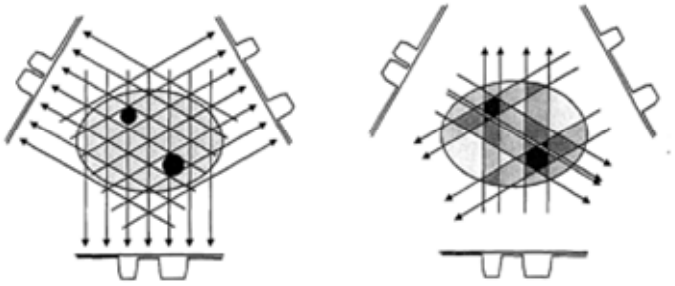
The Challenged Claims relate to the optimization of radiotherapy treatment plans delivered by a medical linear accelerator ("LINAC"). Ex. 1021 ¶¶10-84.

The major components of a radiotherapy treatment machine included a LINAC and a multi-leaf collimator ("MLC"). *Id.* ¶¶15-24. The MLC is affixed to the LINAC and has several sets of metallic leaves that can be moved to create an opening that shapes the beam of radiation as it exits the treatment machine. *Id.* ¶¶28-33. Variously shaped beams can be precisely directed to a patient on a treatment couch from various directions. LINACs have been used to treat patients with radiation therapy in this manner since the early 1990s. *Id.* ¶29

Such conformal radiation treatment requires developing a detailed treatment plan based on three-dimensional images of the patient, which is computationally intensive and mathematically challenging. Intensity Modulated Radiation Therapy (IMRT) is a type of conformal radiation therapy that not only conforms the beam to the shape of a tumor, but also modulates the intensity of radiation delivered to the

[1] https://iopscience.iop.org/issue/0031-9155/46/7 (Last accessed October 4, 2019).

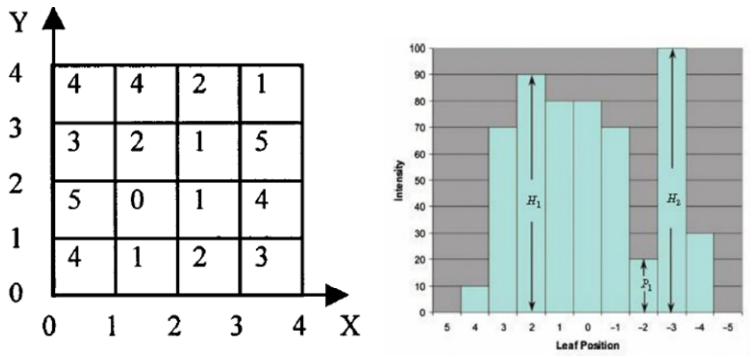
patient on a scale that is smaller than the radiation beam itself (i.e., it converts a single beam into multiple sub-beams, called beamlets), usually by delivering several differently shaped beams from each of several angles. Ex. 1021 ¶¶22-23; Ex. 1003 ¶109; Figure A (shown below).



Beginning in the early 1990s, 3D radiation therapy treatment planning focused on finding beamlet weights that give the best IMRT treatment plan. Ex. 1021 ¶53. But the new IMRT plans were often not practical because they would require too much time for delivery. Ex. 1003 ¶133. Long treatment times are not tolerated well by patients, and not possible for busy treatment centers having many patients to be treated. *Id.*

Therefore, since the mid-1990s, IMRT treatment planning has also considered delivery constraints. Ex. 1003 ¶133; Ex. 1021 ¶84. "Leaf sequencing" algorithms optimize the order of delivery of the MLC fields in the treatment plan (known as "segments") in view of such constraints, to reduce treatment time and make delivery more efficient. Ex. 1003 ¶134. In 2001, Dai *et al.* introduced the concept of complexity and studied its effects on IMRT planning. Ex. 1030 Abstract. They

measured complexity as the number of contiguous "blocks" in an intensity matrix (as shown below Ex. 1003 ¶117) that have the same intensity level.



Dai 2001, and others, considered how treatment delivery time and other aspects of the treatment plan depended on the complexity of the intensity field. *Id.* ¶141.

Sequencing algorithms were initially applied after the process of defining the intensity maps for each beam. But it was known by 2002 that there was a trade-off between optimizing the dose and optimizing delivery, and that optimizing dose and delivery together could provide control over the relative quality and efficiency of the plan. Ex. 1003 ¶¶135-139; e.g., Ex. 1006 (hybrid cost function "X.")

The '175 patent relates to this aspect of IMRT treatment planning, namely, the "user control of the tradeoff, or correlation, between the factors of treatment plan efficiency and dosimetric fitness to optimize a radiation therapy, or radiotherapy, plan," including by use of a hybrid cost function. *Id.* at1:29-32.

VI. BACKGROUND

A. Overview of the ’175 Patent

The ’175 patent describes “controlling the tradeoff between delivery efficiency and dosimetric fitness in radiation treatment plans.” Ex. 1001 2:8-20.

“Delivery Efficiency” is “defined and quantified in terms of ‘Segmentation Count’ and ‘Total Monitor Units.’” *Id.* 2:23-24. “Segment Count” is the “number of required segments.” *Id.* 2:27-28. “Beam on time is proportional to Total Monitor Units required for treatment delivery.” *Id.* 2-34 -35. Accordingly, “total Monitor Units are a quantitative measure of Delivery Efficiency.” *Id.* 2:20-21. “Dosimetric Fitness may be quantified with reference to ‘Dosimetric Cost.’” *Id.* 2:23-24. In IMRT, The Dosimetric cost is used to “quantif[y]” “the fitness of a dose distribution, [and]. [d]ose distributions with low Dosimetric Cost are generally deemed superior to those with a high Dosimetric Cost.” *Id.* 2:23-24. Thus, “Dosimetric Cost” is inversely related to “Dosimetric Fitness.”

The ’175 patent states that it provides a “user control” “of the tradeoff between dosimetric fitness and delivery efficiency” by first, “ providing user control of the segment count in a treatment plan… wherein a delivery cost term based upon the complexity of the intensity maps may be utilized… to drive[] the optimizer toward a simpler, more efficient solution,” second, “providing user control in a treatment plan… of total monitor units” and third, “choosing an optimization algorithm as a

method of controlling treatment efficiency. Specifically, gradient descent and simulated annealing are compared in terms of dosimetric cost and delivery efficiency." *Id.* 2:23-24.

A. Relevant Prosecution History

U.S. Patent Application No. 10/887,966 ("the '966 application"), which resulted in the '175 patent, was filed on July 9, 2004. Ex. 1002 1.

In response to an Office Action dated May 3, 2006, the applicant canceled all seventeen original claims and submitted new claims 18-38. *Id.* 178-198. Applicant also amended the specification to incorporate by reference U.S. Patent Nos. 6,038,283 and 6,393,096. *Id.*

The Examiner issued a final Office Action dated October 25, 2006, rejecting claims 18-38 as unpatentable over *Pirzkall et al.* in view of PCT Publication WO 02/49044 to Alber ("*Alber*"). *Id.* 220-232.

In response, the applicant amended claims 18, 20, 21, 24, 28, 29, and 35, and cancelled claim 19, incorporating the subject matter of this claim into claim 18. The applicant argued that the Examiner had failed to make a prima facie case of obviousness (as required), and that *Pirzkall et al.* and *Alber*, alone or in combination, do not teach or suggest the following elements:

> (1) "providing control of a trade-off between treatment plan dosimetric fitness and delivery efficiency within an optimizer or within the optimization loop to optimize a radiation treatment plan within a

> continuum between delivery efficiency and dosimetric fitness," as recited in [issued claim 1];
>
> (2) "applying prescription parameters to each of a plurality of optimization algorithms within an optimizer, and selecting one of the plurality of algorithms through the optimizer responsive to a user selection between enhanced delivery efficiency and enhanced dosimetric fitness," as recited in [issued claim 1];
>
> (3) "assigning a delivery cost term within an optimizer to each of a plurality of intensity maps representing a potential radiation beam arrangement, and evaluating an objective cost function for each of the plurality of intensity maps," as recited in [issued claim 1]; and/or
>
> (4) "evaluating within an optimizer for each of a plurality of intensity maps an objective cost function including a dosimetric cost term and a the delivery cost term, and rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value," as recited in [issued claim 19].

Id. 251-275, 373.

The applicant also included a declaration by Mark P. Carol, a founder of Nomos Corporation, commenting on the novelty of the claims. *Id.* 279-359.

In this declaration, Mark Carol declared that the "impetus for the Romesberg patent was to propose for the first time the concept of giving the user the ability to control directly on a patient-by-patient basis the competing needs of conformality / avoidance (dosimetric fitness) and efficiency," by "adding a delivery cost term in the cost function that quantifies plan efficiency." Carol also declared that "[t]his term may access the number of segments required to deliver a plan, thus driving a plan toward the use of a smaller number of simpler segments, or it may evaluate the total number of monitor units required to deliver the plan, thus driving the plan toward

requiring less radiation, and therefore less machine time." Carol further declared that the claimed invention,

> not only add[ed] a term to the cost function that quantifies efficiency but it also gives the user the ability to indicate the relative importance of this term as compared to dosimetry fitness, i.e., through the use of a GUI slider bar or other interface known to those skilled in the art, enabling user control of the trade-off between dosimetric fitness (cost) and delivery efficiency (cost) across a continuum.

He opined that "such control [was provided] through user selection of optimization algorithms during a single treatment planning event." More particularly:

> the delivery cost term is not a term quantified directly by the clinician to allow the clinician to determine how fast the plan can be delivered, but is one used by the optimizer to evaluate each potential intensity pattern to thereby determine the optima (best value) of the objective function to determine a beam arrangement (between a continuum of dosimetric fitness and delivery efficiency) to be presented to the clinician during the iterative optimization process.

Carol opined that the claimed invention of the '175 patent could be distinguished from the *Pirzkall et al.* reference. He emphasized that "was a co-author" of the *Pirzkall et al.* study, which "compared[d] a number of techniques for delivering IMRT in terms of dosimetrist fitness and delivery efficiency." He also declared that this study

> was designed to analyze the benefits of one category of delivery technique over another, the result of each different category of IMRT and CRT plan providing different yet repeatable results. These categories would not be selected by an optimizer; rather the category of delivery would be selected by the user before the start of planning,

> would be held fixed throughout optimization, and would not be changeable during the optimization… the choice of techniques had no impact on the optimizer whatsoever other than to determine the location of the beam directions used to treat the patient.
>
> . . . [t]he planning system… [in the Pirzkall Study] provided no means for impacting, controlling, or modifying efficiency nor did it even recognize that this would be of value; ***the planning system always tried to create the best plan possible given the dosimetric requirements of the user as inputted into the planning system regardless of how long it took to deliver it***. Efficiency was evaluated after plan creation by the user and was found to be associated with the technique used for delivering a plan--CRT was found to be the most efficient regardless of dosimetric quality, where noncoplanar fixed fields was found to be the least efficient regardless of dosimetric quality.

Carol emphasized that "although *Pirzkall et al.* evaluated efficiency and showed how one technique of delivery may be more efficient than another, it does not recognize the need for nor propose a means of trading off efficiency against dosimetric quality on a patient-by-patient basis."

Carol also opined that the claimed invention of the '175 patent could be distinguished from the *Alber* reference. Carol declared that the *Alber* reference "attempts to address" the fact that "the theoretical model of the delivery equipment resident within the planning system is not an exact duplicate of the actual device used to treat the patient," by

> providing a means for adjusting the plan as it is created so that it converges on a dose distribution that represents more accurately the dose that will actually be delivered by the equipment. That is, there is a component of the Alber cost function that takes into account the differences between the ideal solution created by the planning system and the actual practical implementation that will result (segments, field

> shape, number of MUs, time to move the MLC leaves, etc[.]) when it is delivered.

Carol emphasized that with the *Alber* approach (i) "there is no means suggested, described, or provided that allows the user to control this convergence from ideal to practical; it is hard-wired into the algorithm proposed in the invention, and (ii) "this approach does not take into account in any way, shape, or form, the issue of efficiency. While it is true that at times the solution that is arrived at by the algorithm may be more efficient than one that did not converge in the proposed manner, there is no expectation that this will happen."

Carol further declared that Alber

> describe[d] and provide[d] a solution to the problem of differences between theoretical plans and delivered plans. It does not recognize the need for nor propose a means of trading off efficiency against dosimetric quality. The Alber algorithm always tries to create the plan that best represents the dose that will actually be delivered without any consideration given to, or recognition of the value of evaluating how long it will take to deliver the plan.

Thereafter, the Examiner allowed claims 18, 20-38 of the '966 application. The Examiner provided the following rationale for allowing these claims:

> (1) The prior art does not teach or fairly suggest the method wherein the cost function includes both the dosimetric cost term and the delivery cost term, and wherein the evaluation of the delivery cost term for each of a plurality of respective intensity maps has linear computational complexity with respect to the size of the respective candidate intensity map as recited in [issued claim 1];
>
> (2) The prior art fail to teach or suggest the method wherein the plurality of algorithms within the optimizer includes both the local and the global optimization algorithms so that the user selects between

> enhanced delivery efficiency and enhanced dosimetric fitness as recited in [issued claim 11]; and
>
> (3) The prior art fail to teach or suggest the method wherein the delivery cost term is assigned to each of a plurality of intensity maps based on the respective complexity of each intensity map, and wherein the cost function includes both the dosimetric cost term and the delivery cost term, in the manner required by [issued claim 13].
>
> (4) The prior art fail to teach or suggest the method wherein the objective cost function includes both a dosimetric cost term and a delivery cost term, in the manner recited by [issued claim 19].

Contrary to this conclusion, the prior art references (individually or in combination) relied upon in this Petition disclose or suggest a "cost function [that] includes both the dosimetric cost term and the delivery cost term" and "user control of the tradeoff, or correlation, between the factors of treatment plan efficiency and dosimetric fitness to optimize a radiation therapy, or radiotherapy, plan."

B. Cited References

1. Shepard 2002

Shepard 2002 discloses that "[Nomos] CORVUS makes use of the traditional two-step approach to inverse planning in which an optimized pencil beam intensity pattern is translated into a set of deliverable apertures." Ex. 1010 1013. Shepard 2002 then compares "CORVUS" with a new approach called "DAO" (as shown in Figure 16below) to "illustrate the extent to which DAO can reduce the number of segments and the required number of monitor units to deliver a step-and-shoot plan." Ex. 1010 Fig. 16 and Table III; Ex. 1003 ¶¶ 216-223.

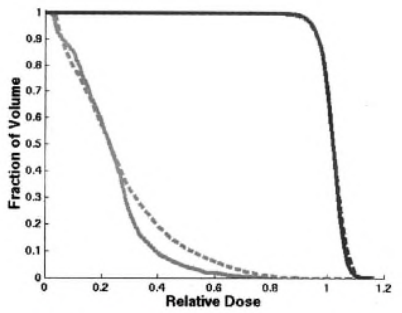


FIG. 16. A DVH comparison of the results produced by direct aperture optimization (solid lines) and the corresponding results produced by CORVUS (dashed lines).

	Direct aperture optimization	CORVUS
Total No. of segments	21	144
Total No. of monitor units	500	1860

Table III.

2. Que 1999

Que 1999 compares the performance of eight different "field segmentation" algorithms that "translate[] beam intensity maps into the least number of MLC field segments," including "the ones by Bortfeld et al., Galvin et al., Xia and Verhey, the Siemens IMFAST algorithm, and four other algorithms which have not been studied before." *Ex. 1012* Abstract.

Que 1999 compares these algorithms with plots that show the average number of segments and fluence required for the treatment plans depending on the number of intensity levels (Figures 1 to 4). Que 1999 also compares these algorithms with charts that show how they performed for ten clinical cases, with the results of the

algorithms having the smallest number of segments indicated in boldface (Tables I-III).

Que 1999 concludes, "[I]t is desirable to have multiple algorithms available in a clinical treatment planning system which will search through all algorithms automatically and find the most efficient delivery sequence for a given treatment. Each intensity map in a treatment could be delivered by a different algorithm, whichever is the most efficient for that map." *Id.*; Ex. 1003 ¶¶ 224-228.

3. Webb 2001

Webb 2001 notes that many treatment planning systems at that time produced plans with high dose-space conformality," but that their "monitor-unit efficiency" could be "quite small."

Webb 2001 addresses this "tradeoff between obtaining desirable features in beam-space and high conformality in dose-space." *Id.* Abstract. More specifically, Webb 2001 provided a mechanism by which "this can be under the control of the user." Ex. 1006 N188. Webb 2001's "*new development* [wa]s to compute two extra parameters at each iteration[,] which characterize beam-space and then make use of them in a hybrid cost function," as shown below. *Id.* N189.

$$\chi = \left\{ \sum_i \sum_j I_w(i,j)(D(i,j) - D^p(i,j))^2 \right\} + w_3[w_1 S_+ - w_2 F_{\min}].$$

Webb 2001's hybrid cost function includes weighting parameter w_3, which controls the relative contribution of the beam-space term relative to the dose-space term. *Id.* N190. The weight "can be set by a user" and it "allows the user to choose between the degree of conformality and the degree of smoothness and size of field components in the constituent beams." Ex. 1003 ¶¶195-203.

4. Bar 2001

Bar 2001 describes "a step and shoot sequencer . . . that can be integrated into an IMRT optimization algorithm." Ex. 1014 Abstract. The sequencer "can be integrated into the optimization process of our treatment planning program. It considers all technical limitations of the MLC." *Id.* 1998:2. "The result of the optimization process is a quasicontinuous fluence weight profile for every beam orientation." *Id.* 1998:5. "The sequencing process of converting the optimized profile into segments has to balance two important strands of the treatment. On one hand, the sequencing should translate the original profile as closely as possible to avoid serious deterioration of the treatment plan. On the other hand, the number of segments should be as small as possible because segment number strongly influences the treatment time." *Id.* 1997:3-1998:1. These balancing strands are comparable to delivery efficiency and dosimetric cost of the '175 patent. *See also* Ex. 1003 ¶¶ 204-209.

5. Siebers 2002

Siebers 2002 describes an "in-house IMRT system" that was "modified to include the calculation of the deliverable intensity into [sic] the optimizer." It explains that "[i]n this process, prior to dose calculation, the MLC leaf sequencer is used to convert intensities to dynamic MLC sequences, from which the deliverable intensities are then determined." Ex. 1008 Abstract. Siebers 2002 uses "a simple method to incorporate beam delivery constraints into the IMRT optimization process," in which "the beam delivery constraints are accounted for in the fluence to trajectory or MLC leaf sequencing conversion program." *Id.* 953; Ex. 1003 ¶¶ 210-215.

VII. PERSON OF ORDINARY SKILL IN THE ART ("POSITA")

The level of skill in the art is generally evidenced by the prior art references. *Chore-Time Equip., Inc. v. Cumberland Corp.*, 713 F.2d 774, (1983); *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (2001). A POSITA, would have an undergraduate degree in science, computer science, engineering or math, and an advanced degree in radiation dosimetry, physics, medical physics, medicine, or an equivalent field of study, with some clinical experience in radiotherapy treatment planning. Ex. 1003 ¶¶55-98

VIII. CLAIM CONSTRUCTION (37 C.F.R. § 42.104(B)(3))

Petitioner submits that the claims be construed in accordance with their ordinary and customary meaning as understood by one of ordinary skill in the art and the prosecution history and submits the following constructions:

A. "total monitor units"

Claim Limitation	***Proposed Construction***	***Claims***
"total monitor units"	"the total radiation beam on time of the linear accelerator used in providing the treatment"	8, 10, 19, 20

A person of ordinary skill in the art ("POSITA") would understand that the limitation "total monitor units" as used in the claims of the 175 patent means "a portion of a radiation beam arrangement." Ex. 1003 ¶¶175, 176-182. The POSITA would recognize that the '175 Specification provides an express definition for this limitation and that this definition is consistent with how the limitation is used in the claims. *Id.* 176-179.

This express definition is consistent with the use of this term in the claims of the '175 patent. Ex. 1001, claims 8, 9 ("delivery efficiency is represented by total monitor units to deliver the radiation treatment plan.") Thus, "Total Monitor Units" is a quantifiable representation or measure to deliver radiation according to a radiation treatment plan.

The Specification also makes clear that "Total Monitor Units" is a measure or representation of treatment time. *Id*. FIGS. 7, 8, 3:64-4:05. The association of "Total Monitor Units" to the amount of treatment time was further reinforced during prosecution by the assertion that:

> "IMRT is inherently an inefficient process. It uses a large number of beam segments (small portions or pieces of a large beam) each controlled individually and ***each delivered for a certain amount of time (equivalent to the number of monitor units of beam-on time***). . . ."

Ex. 1002, '175 (Carol Decl.) p. 3. Thus, a POSITA would construe "***total monitor units***" as "t***he total radiation beam on time of the linear accelerator used in providing the treatment***" which is a certain amount of time to deliver radiation.

B. "segment count"

Claim Limitation	***Proposed Construction***	***Claim***
"segment count"	"the number of segments required by a treatment plan for delivering radiation" (i.e., "the number of required segments")	17

The '175 patent provides the POSITA with an explicit definition of the claim limitation "Segment Count," namely, "*the number of segments required by a treatment plan for delivering radiation" (i.e., "the number of required segments."*). Ex. 1001 2:23-28. ." Ex. 1003 ¶¶183-188. This construction is consistent with the use of this limitation in the claims. *Id*. claim 17 ("the delivery cost term represents a segment count; and… a delivery cost not exceeding a predetermined segment count

and having a minimal dosimetric cost.") The definition of "Segment Count" also explains why a smaller segment count indicates a more delivery efficient treatment plan. Because a beam segment is a small portion of a large beam, fewer segments required to deliver a plan, the more efficiently the radiation treatment plan can be applied to a patient. Ex. 1002 (Carol Decl.) p. 3. Thus, a person of ordinary skill in the art would understand from reading the patent that Segment Count is a "***number of segments required by a treatment plan for delivering radiation"*** to a patient.

C. "optimizer"

Claim Limitation	***Proposed Construction***	***Claim***
"optimizer"	"an iterative optimization loop	17

The'175 patent uses does not define the term "optimizer," which is used in the claims and the summary section that parrots the language of the claims. Ex. 1003, ¶¶189-194; Ex. 1001 1:41-42, 44-47.

However, during prosecution, the patentee repeatedly discussed the claims through this term and provided an express definition for "optimizer." Specifically, patentee repeatedly distinguished the claims of the '175 patent from the prior art cited by the examiner by asserting that the cited prior art "does not disclose, teach, or suggest providing control of a trade-off. . . within an optimizer or within the optimization loop. . . ." *Id*. ¶¶190-192. This assertion, equating "within an

optimizer" to "within the optimization loop," was repeated made during prosecution to distinguish the claims from the cited art. *Id.* Further, during prosecution, it was explained that "within the optimizer or optimization loop" is an iterative looped process. *Id*. ¶193.

ARGUMENTS

The Challenged Claims are unpatentable in view of the references cited for each ground below.

Grounds	´175 Patent Claims	Basis for Unpatentability
Ground I	Claim **1**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Webb 2001** (Ex. 1006)
Ground II	Claim **13**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Webb 2001** (Ex. 1006) in view of **Bar 2001** (Ex. 1014)
Ground III	Claim **17**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Webb 2001** (Ex. 1006) in view of **Bar 2001** (Ex. 1014) and further in view of **Shepard 2002** (Ex. 1010)
Ground IV	Claim **8**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Webb 2001** (Ex. 1006), in view of **Bar 2001 (**Ex. 1014) alone or further in view of **Siebers 2002** (Ex. 1008)
Ground V	Claims **10**, **19**, **20**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Webb 2001** (Ex. 1006), in view of **Bar 2001** (Ex. 1014), further in view of **Siebers 2002** (Ex. 1008) and further in view of **Shepard 2002** (Ex. 1010)
Ground IV	Claims **11**, **12**	Obvious under 35 U.S.C. § 103 (pre-AIA) over **Shepard** (Ex. 1010), in view of **Que 1999** (Ex. 1012)

IX. GROUND I: WEBB 2001 (CLAIM 1)

Claim 1 is unpatentable as obvious at least in view of Exhibit 1006 (Webb 2001.)

A. Claim 1 (preamble): "A method of determining a radiation beam arrangement, the method comprising the steps of…"

Exhibit 1006 (Webb 2001) discloses "a method of determining a radiation beam arrangement" as recited in the preamble of claim 1. In Webb 2001, "[d]elivery of intensity-modulated radiation beams (IMRT) is known to improve the conformality of external-beam radiation therapy. There is a vast literature on the planning and delivery of IMRT (*see*, for example, reviews by Webb (2000a))." Ex. Ex. 1006 N187 ¶1. Webb 2001 acknowledges that "there are today a large number of planning and delivery techniques… [where] [m]odulated beams created by inverse-planning systems are 'interpreted' into MLC leaf patterns which, when delivered, create a close approximation to the computed dose distribution." *Id*. N188 ¶2. "Inverse planning has been carried out iteratively using the technique described by Webb et al (1998). This is an iterative method which predetermines the number of coplanar gantry angles and creates the modulated 1D profiles which, when combined, lead to a conformal 2D dose distribution. . . [where] . . . the outcome is a set of beam profiles and the corresponding dose distributions together with statistics characterizing the distribution including the appropriate dose-

volume histograms." *Id*. N188 ¶5. A POSITA would, therefore, understand that Webb 2001 describes an iterative inverse planning method and that the described "outcome" of "a set of beam profiles and the corresponding dose distributions together with statistics characterizing the distribution including the appropriate dose-volume histograms" is a "radiation beam arrangement" that is "determined" by iteratively using the described "hybrid cost function," which is "[a] very simple cost function at the heart of an iterative algorithm for computing IMBs [that] allows the user to choose between the degree of conformality and the degree of smoothness and size of field components in the constituent beams. . .[which] method is very transportable..." *Id*. N194 ¶2; Ex. 1003 ¶¶264-269.

Claim 1 [a]: "receiving prescription parameters for a patient target; and"

Webb 2001 (Ex. 1006) discloses the limitations of claim 1[a] or it would at least be obvious to a POSITA in view of Ex. 1006.

Webb 2001 discloses: "[i]nverse plans were constructed for the model problem shown in figure 1 for a range of user-selected parameters shown in table 1 [where] [t]he results demonstrate the ability to 'control' the outcomes through appropriate choice of parameters." Ex. 1006 at N190 ¶3, N191 (Table 1).

Table 1. The parameters applied during the optimization and the consequent outcomes in dose-space and beam-space for 11 separate optimizations. All symbols and the results are discussed in the text.

	9 beams equispaced at 40° intervals					5 beams equispaced at 72° intervals					
Run	4	1	8	10	9	12	13	14	15	16	17
Cost in dose space	4329	4861	5725	7029	8800	5497	6334	6656	6867	7235	8134
Cost in beam space	—	—	−7.0	−16.2	−24.2	—	—	1.1	−1.0	−1.9	−6.1
w_1	—	—	0.1	0.1	0.1	—	—	0.1	0.1	0.1	0.1
w_2	—	—	1	1	1	—	—	1	1	1	1
w_3	0	0	10	20	30	0	0	10	20	30	50
MWF included?	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
OAR_{mean}	0.285	0.312	0.418	0.493	0.560	0.365	0.402	0.435	0.453	0.475	0.523
σ_{OAR}	0.238	0.257	0.216	0.202	0.191	0.240	0.259	0.244	0.239	0.233	0.214
PTV_{mean}	0.996	0.996	0.995	0.993	0.993	0.995	0.992	0.993	0.992	0.991	0.988
σ_{PTV}	0.026	0.024	0.023	0.021	0.023	0.025	0.026	0.026	0.025	0.023	0.024
S_+	364	273	250	228	218	330	274	241	240	231	219
F_{min}	11	27	32	39	46	7	19	23	25	25	28
V_{80}	0.067	0.076	0.087	0.115	0.132	0.078	0.102	0.121	0.123	0.128	0.147
V_{70}	0.094	0.110	0.125	0.179	0.216	0.126	0.149	0.165	0.176	0.189	0.232
V_{60}	0.124	0.149	0.182	0.242	0.313	0.178	0.215	0.237	0.247	0.261	0.294

Ex. 1006 (Table 1)

A POSITA would understand or find it obvious that the "parameters" identified in Table 1 (Left Column) are associated with a patient and, therefore, are "*parameters for a patient target*" as recited in claim 1[a]. I*d.* N188 ¶3, N189 ¶1. These "parameters" are "applied during optimization" using "a hybrid cost function χ. *Id*. N189 ¶¶3-4, N190 ¶1 (*Equation 2*:

" $\chi = \left\{\sum_i \sum_j I_w(i,j)\left(D(i,j) - D^p(i,j)\right)^2\right\} + w_3[w_1 S_+ - w_2 F_{min}]$") The left portion of Equation (2) is a cost function for optimizing conformity in the dose-space with the "outcome [being] a set of beam profiles and including the corresponding dose distributions." *Id*. 188 ¶¶5, 6, N189 ¶1 ("2. Method" section). A POSITA would understand that the "importance factors," "dose from the grains so far," and "the prescribed dose distribution" for PTV and OARs this section of

Webb 2001 are "***prescription parameters for a patient target***" as recited in claim 1[a]. Ex. 1003 ¶¶271-276.

Webb 2001 also discloses ***"receiving"*** the prescription parameters for a patient target in the manner recited in claim 1[a], or at least that it would be obvious to POSITA from reading Webb 2001 . These parameters are "user selected" choices (Ex 1006, Table 1) in order to construct inverse plans for the model program shown in Figure 1. *Id*. N190 ¶3 ("Inverse plans were constructed for the model problem shown in figure 1 for a range of user-selected parameters shown in table 1. The results demonstrate the ability to 'control' the outcome through appropriate choices of parameters"). The exact parameters required [by the described hybrid cost function] become user-definable tools. . ." and "parameters [are] applied during the optimization…" *Id*. N194, N191. Taking these statements together, a POSITA would understand that the ability for a user to select the parameters used in the described hybrid cost function for computing outcomes, means that these user-selected parameters are received into (*i.e.*, provided to) the hybrid cost function in order to compute outcomes based on the cost function. Ex. 1003 ¶¶ 270-279.

Claim 1 [b] "evaluating a cost function for each of a set of a plurality of candidate intensity maps formed responsive to the prescription parameters to provide control of a trade-off between treatment plan delivery efficiency and dosimetric fitness within an optimizer to optimize a radiation treatment plan within a continuum between

substantially optimal dosimetric fitness and enhanced delivery efficiency at an expense of dosimetric fitness,"

Ex. 1006 discloses claim step 1[b]. A POSITA would understand that the "hybrid cost function" described in Webb 2001 (N189 Equation (2), below) corresponds to the "***cost function. . .*** " recited in claim 1[b] because this equation "combines features from dose-space and [] features from beam space" (Ex. 1006 N189 ¶4):

$$\chi = \left\{ \sum_i \sum_j I_w(i,j)(D(i,j) - D^p(i,j))^2 \right\} + w_3[w_1 S_+ - w_2 F_{\min}]$$

The "dose-space" term, on the left in braces, is used to define the dose at each voxel in a patient model. The "beam space" term, on the right, addresses features relating to its delivery by a radiation therapy machine. Ex. 1003 ¶282.

Webb 2001 discloses "***evaluating***" this cost function in its "3. Results" and "4. Discussion and conclusions" sections and Table 1 and Figure 2. (Ex. 1006 N190 – N194), as recited in claim 1[b]. Equation (2) is "…***formed responsive to the prescription parameters***…" Ex. 1006 N190 ("Inverse plans were constructed…for a range of user-selected parameters shown in table 1."); N191 ("The parameters applied during the optimization and the consequent outcomes in dose-space and beam-space for 11 separate optimizations").

Webb 2001's hybrid cost function is repeatedly described as enabling user control of a tradeoff between desirable beam space properties and conformal dose-space conformality in the manner recited in claim 1[b]. Ex. 1006 at: N188 ¶4 ("Inevitably we shall find that a tradeoff arises. It will be shown how this can be under the control of the user."); N190 ¶3 ("…a range of user-selected parameters shown in table 1. The results demonstrate the ability to 'control' the outcome through appropriate choices of parameters."); N187 Abstract ("There is a tradeoff between obtaining desirable features in beam-space and high conformality in dose-space"); N194 ¶2 ("In this note it has been shown how the desirable features of beam-space may be traded off with the degree of conformality in dose-space. A very simple cost function at the heart of an iterative algorithm for computing IMBs allows the user to choose between the degree of conformality and the degree of smoothness and size of field components in the constituent beams. The exact parameters required become user-definable tools and depend on the number of fields contributing to the plan."); Ex. 1003 ¶¶284-286. Further, the above excerpts indicate, a POSITA would understand "degree of conformality" in Webb 2001 corresponds to "***dosimetric fitness***" recited in claim 1[b]. *Id*. A POSITA would also understand "high conformality in dose-space" corresponds to the recited "***substantially optimal dosimetric fitness***." *Id*.

A POSITA would also understand "desirable beam-space properties" in Ex. 1006 to be the recited ***"treatment plan delivery efficiency."*** Ex. 1006 N188:4; N187 Abstract. Further, a POSITA would understand that the discussion of trade-off mentioned in Webb 2001 discloses ***"provid[ing] control of the trade-off . . . to optimize a radiation treatment plan within a continuum between substantially optimal dosimetric fitness and enhanced delivery efficiency at an expense of dosimetric fitness***" as recited in claim step 1[b]. The "continuum" is indicated, for example, by the use of the weighting factor w_3. Webb 2001 N190 ¶1 (description of w_3). The POSITA would understand that $w_3 = 0$ defines one end of the bounded continuum of "substantially optimal dosimetric fitness" provided by the cost function of Equation (1). *Id*. N188; N190 ¶4 ("The first column [in Table 1] is a baseline plan with no attempt made to manipulate beamspace (i.e. w3 = 0 and no MWF). It produces the lowest value of the dose-space cost function χ."). Similarly, larger values of w_3 approach the other end of the continuum where increasing w_3 leads to a loss (or expense) in dosimetric fitness as required by the claim limitation. *Id*. N190 ¶1 ("For non-zero w_3 there is a contribution from the cost of beam-space. The larger the value of w_3 the more the iteration is weighted towards the demands in beam-space. It will be shown that as w_3 increases the IMBs become smoother and the maximum value of the minimum fieldsize increases as desired. However, some conformality in dose-space is inevitably lost. The relative weights of w_1 and

w_2 control whether beam smoothing or maximization of minimum fieldsize is the priority."); Ex. 1003 ¶¶287-289.

Figure 2(a) shows the results "when only dose-space cost is considered" and Figures 2(b) shows the results "when dose-space and beam-space cost are considered." *Id*. N192 (Text accompanying Figure 2). When the weight of the beam-space term is selected to $w_3 = 0$, "the iterations ignore beam-space constraints and proceed to minimize only the cost in dose-space as in equation (1)," with results as shown in Figure 2(a). *Id*. 190 ¶1. When the user selects the weight of the beam-space term to be "non-zero" "there is a contribution from the cost of beam-space. The larger the value of w_3 the more the iteration is weighted towards the demands in beam-space." *Id*. A POSITA would also immediately recognize that Figure 2(a) and (b) of Webb 2001 are strikingly similar to the images in FIGS. 2 and 4 of the '175 Patent, both depicting beam maps that demonstrate the trade-off. Ex. 1003 ¶294.

Control of the trade-off based on adjusting w_3 is further shown in Table 1: "Columns 3-5 show the effect of increasing the weight to the contribution from beam-space to the cost function χ. As w_3 rises. . . the cost in dose-space rises, the mean dose to organs at risk rises, the PTV dose is maintained but, as demanded, the beam-space characteristics dramatically improve… It may be seen that as the beam-space characteristics improve [the values representing fractions of the OAR

volume above 60, 70, and 80% of the mean PTV] rise again, reflecting the poorer conformality." *Ex. 1006* N190 ¶4.

Webb 2016 also "***provid[ing] control of the trade-off . . . within an optimizer...***" Ex. 1006 N194 ¶4 ("The field of optimization of IMRT is increasingly moving towards these notions of including all the geometrical and dosimetric features inside the optimization itself") *Id*. N194 ¶2 (""allows the user to choose between the degree of conformality and the degree of smoothness and size of field components in the constituent beams [through] user-definable tools . . ."Thus POSITA would know from Ex. 1006 how to control of the tradeoff between dose space and beam space parameters occurring within the optimizing software (e.g., an optimizer) or that it would be obvious to do so given the recognition in Ex. 1006 that the described hybrid algorithm is highly transportable into treatment planning software of commercial manufacturers.

Also, the POSITA would understand that Webb 2001 discloses **"**(*evaluating a cost function). . .* ***for each of a set of a plurality of candidate intensity maps formed responsive to the prescription parameters***." Webb 2001's hybrid cost function is used in an iterative optimization process in which the cost function is evaluated repeatedly, at each of potentially many iterations, for the intensity map being considered at that iteration, given the model parameters. The "3. Results" section of Webb 2001 discloses an evaluation of the cost function for each of a set

of a plurality of candidate intensity maps formed responsive to the prescription parameters with reference to Table 1 (Ex. 1006. N190 ¶4 and N192-N193 (Figure 2):. "Table 1 shows the results. Five plans (labelled runs 4,1,8,10,9) were computed, each with nine equispaced IMBs." A POSITA would understand that Table 1 shows, for each of 11 runs: the calculated value of the dose-space term, the calculated value of the beam-space term, the set values of the three weights, statistics for the calculated partial volumes (e.g. the target, an OAR), the calculated value of the two delivery cost component terms, and three DVH points. *See* Ex. 1003 ¶¶ 280-296.

Claim 1 [c] "the cost function including a dosimetric cost term representing dosimetric cost and related to dosimetric fitness of the respective candidate intensity map and a delivery cost term representing delivery cost and related to delivery time to deliver radiation according to a beam arrangement represented by the respective candidate intensity map,"

The POSITA would understand that Webb 2001 discloses claim 1[c]. The hybrid cost function "χ" (Equation (2)) is a cost function that has both of the elements of the cost function recited in claim step 1[c]. *See* Ex. 1006 189 ¶2-N190 ¶3.

$$\chi = \left\{ \sum_i \sum_j I_w(i,j)(D(i,j) - D^p(i,j))^2 \right\} + w_3[w_1 S_+ - w_2 F_{\min}]. \qquad (2)$$

The left side portion of the hybrid cost function would be understood by the POSITA as the "***dosimetric cost term***" and ***"represent[s] dosimetric cost and [is]***

related to dosimetric fitness of the respective candidate intensity map" as recited in claim 1. *See* Ex. 1006 (Webb 2001) N190 ¶1 ("if w_3 is set to zero the iterations ignore beam-space constraints and proceed to minimize only the cost in dose-space as in equation (1)."). The POSITA would also understand that the right side portion of the hybrid cost function: "$w_3[w_1 S_+ - w_2 F_{min}]$" that concerns "beam-space cost" is "***a delivery cost term***" and "***represent[s] delivery cost and [is] related to delivery time to deliver radiation according to a beam arrangement represent by the respective candidate intensity map***" as recited in claim 1[c]. *See*, Ex. 1006 Webb 2001 N189 ¶2-N190 ¶4 (Discussing the two parameters in the "beam-space" for improving "delivery efficiency": S_+ and $F_{\min}$.).

The POSITA would know that Equation (2) is used to control the trade-off between "high dose space conformality" and the "monitor efficiency" achieved upon delivery. *Id.* N187(Abstract), N190 ¶1 ("For non-zero w_3 there is a contribution from the cost of beam-space. The larger the value of w_3 the more the iteration is weighted towards the demands in beam-space. It will be shown that as w_3 increases the IMBs become smoother and the maximum value of the minimum fieldsize increases as desired. However, some conformality in dose-space is inevitably lost.").

Further, from the description of Webb 2001, the first component of the beam-space term (shown below) is described as pertaining to "smoothing" and is the "sum S_+ … of the positive going fluence changes. . . ."

$$S_+ = \sum_{n=1}^{N_B} \sum_{m=1}^{20} (\Delta_+ I)_{m,n}$$

Id. 189 ¶2. The second component of the beam-space term (shown below) relates to "field size" and is the "sum over all beams of these values $F_{\min}$."

$$F_{\min} = \sum_{n=1}^{N_B} [\max(d_{\min})]_n$$

Id. 189:3. The POSITA would understand that the "sum *S*+" and "sum over all beams of these values $F_{\min}$" pertain to delivery efficiency: "The relative weights of w_1 and w_2 control whether beam smoothing or maximization of minimum fieldsize is the priority. . . . S_+ has dimensions of fluence which scales to monitor units… $F_{\min}$ has dimensions of length (cm) and the quadratic dose term is dimensionless since we seek unity dose in the PTV. In this way the hybrid cost function will control the behaviour in the two spaces (dose-space and beam-space) according to the weights w_1, w_2, w_3 which were adjusted to reflect the dimensions of S+ and Fmin." Ex. 1006 N190 ¶1; N190 ¶4 (reported results.); Ex. 1003 ¶¶297-307.

Claim 1 [d] "the evaluation of the delivery cost term for each respective candidate intensity map having linear computational complexity with respect to size of the respective candidate intensity map."

The hybrid cost function (Equation (2)) in Webb 2001 discloses the limitations recited in claim [d]. The "hybrid cost function…control[s] the behaviour in the two spaces (dose-space and beam-space) according to the weights w_1,w_2,w_3 which were adjusted to reflect the dimensions of S_+ and $F_{\min}$." with the right-most portion of the equation comprising the recited "***delivery cost term***" of claim 1, namely: $w_3[w_1 S_+ - w_2 F_{min}]$. Ex. 1006 N189 ¶2-N190 ¶1. From this portion of the hybrid cost function, the POSITA would recognize and understand that the delivery cost term has linear complexity because all of the terms in this portion of the hybrid cost functions are non-exponential, first order terms: $w_3[w_1 S_+ - w_2 F_{min}]$. Ex. 1003 ¶¶308-311. Thus, Webb 2001 renders claim 1 obvious.

X. GROUND II: WEBB 2001 IN VIEW OF BAR (CLAIM 13)

A. Claim 13. "A method of providing control of a trade-off between treatment plan delivery efficiency and dosimetric fitness to optimize a radiation treatment plan within a continuum between delivery efficiency and dosimetric fitness the method comprising the steps of…

As discussed in Section IX.A (esp. with regards to claim 1[b]), Webb 2001 discloses the limitations recited in the preamble of claim 13. Ex. 1003 ¶397.

Claim 13 [a]: "assigning a delivery cost term within an optimizer to each of a plurality of intensity maps representing a potential radiation beam arrangement, the assignment based on complexity of each respective intensity map,"

As discussed above in section IX.A (esp. with regards to claim 1[d])] and incorporated here, Webb 2001 in view of Bar 2002 disclose all of the limitations recited in claim 13[a]. *See* Ex. 1003 ¶¶398-399.

Further, Bar 2001 describes "***assigning a delivery cost term…[w] the assignment based on complexity of each respective intensity map***…". Bar 2001 discloses "a step and shoot sequencer . . . that can be integrated into an IMRT optimization algorithm." Ex. 1014 Abstract. The step and shoot sequencer "can be integrated into the optimization process of our treatment planning program [and] considers all technical limitations of the MLC." *Id.* 1998:2. Bar 2001 developed this sequencer to address the trade-off between dosimetric fidelity and delivery efficiency. *Id.* 1997:3-1998:1 ("The sequencing process of converting the optimized profile into segments has to balance two important strands of the treatment. On one hand, the sequencing should translate the original profile as closely as possible to avoid serious deterioration of the treatment plan. On the other hand, the number of segments should be as small as possible because segment number strongly influences the treatment time."); 1999:4 *(discussing* "additional constraints due to dosimetric concerns" including peaks (with an MLC constraint) and valleys (with a dosimetric constraint.))

According to Bar 2001, integration of the sequencing into the optimization is desirable because it allows the possibility of optimizing the sequencing with

respect to the dose distribution." *Id.* 1998:3, and Abstract. In addition, Ex. 1014 2004-2005 shows how to assign delivery cost terms *based on complexity of each respective intensity map…*" in a manner consistent with claim 13[a]. *Id.* 1999 ("…the last segment is composed of all elements with a maximum fluence value. The minimum fluence value of every segment is assigned to it as monitor units.")

In Table 1 of Bar 2001, assignment of the delivery cost term for each profile is based on complexity of the map as shown by the number of segments and clusters. *See* Ex. 1014 2003 (Table 1) and 2004-2005 (section 3.2 Segmentation), *Id.* 1998 (2.1. Clustering (b)); 1999 (2.2 Segmentation (first paragraph)); 2002 (Figure 2 (discussed at 2001 with regards to the 8 mathematical profiles of varying complexity).. Thus, what happens with segmentation (and clustering) reflects a degree of complexity: The more segments or clusters, the more complex the map. *See* Figure 2 (profiles (i)-(viii) – vi and viii being most complex), Fig. 1; 1998-1999 ("2.1 Clustering – (a)-(c)); 1999-2001 (2.2. Segmentation (a)-(f)). As such, assigning segments or clusters as a delivery cost term as described in Bar 2001 is an "assign[ment of] a delivery cost term…[with] the assignment based on complexity of each respective intensity map…".As Webb 2001's algorithm allows easy adaption for delivery costs terms (on the w_3 side of its equation), it would be easy for a POSITA to combine the teachings of Webb 2001 and Bar 1014 together

to afford the assigning of delivery costs terms based on complexity as recited in claim 13[a]. *See* Ex. 1003 ¶¶401-402.

As to motivation to combine, Bar 2001, describes a step and shoot sequencer that "can be integrated into an IMRT optimization algorithm" *(Ex. 1014* Abstract) that "considers all technical limitations of the MLC." *Id.* 1998. Bar 2002 explains that "integration of the sequencing into the optimization is desirable, because it allows the possibility of optimizing the sequencing with respect to the dose distribution." In view of the above, a POSITA addressing the limitations of claim 13[a] Webb 2001 together with Bar 2001. *Id.* ¶¶400-403.

Claim 13 [b]: "evaluating an objective cost function for each of the plurality of intensity maps, the objective function including a dosimetric cost term and the delivery cost term,"

As discussed above in Section IX.A with regards to claim 1[c], and incorporated here, Webb 2001 discloses these claimed limitations of claim 13[b]. *See Ex. 1003* ¶404.

Claim 13 [c]: "the dosimetric cost term representing dosimetric fitness of the respective intensity map and the delivery cost term representing delivery efficiency."

As discussed above in Section IX.A. with regards to claim 1[c], and incorporated here, Webb 2001 discloses these claimed limitations of claim 13. *See* Ex. 1003 ¶405.

XI. GROUND III: WEBB 2001 IN VIEW OF BAR 2001, IN FURTHER VIEW OF SHEPARD (CLAIM 17)

A. Claim 17 "A method as defined in claim 13 wherein the delivery cost term represents a segment count; and wherein simulated annealing is utilized to form the radiation therapy plan having a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost."

Claim 17: "A method as defined in claim 13 wherein the delivery cost term represents a segment count;…"

Claim 17 of the '175 patent is unpatentable as being obvious over Webb 2001 (Ex. 1006) in view of Bar 2001 (Ex. 1014) and further in view of Shepard 2002 (Ex. 1010). Claim 17 depends from claim 13. *See* Section X concerning claim 13 and incorporated here with respect to the limitation "***A method as defined in claim 13***…" of claim 17. *See* Ex. 1003 ¶406-407.

With respect to the portion of claim 17: "***wherein delivery cost term represents a segment count;…***" it is disclosed by Bar 2001 through its description of "number of segments." *See* Ex. 1014 1998 ¶1 ("the number of segments should be as small as possible because segment number strongly influences the treatment time.") A POSITA understands a "number of segments" corresponds to a segment count and is a delivery cost term. Ex. 1003 ¶¶409-410. Bar 2001's "step and shoot sequencer" that can be "integrated into the optimization process of our treatment planning program" to optimize the number of segments so that "the number of segments should be as small as possible because segment number strongly

influences the treatment time (Que 1999)" would be understood by a POSITA to mean that the "number of segments" as used in Barr 2001 is a delivery cost term representing a number of segment as recited in claim 17. *See* Ex. 1014 1998 ¶¶1-2l, 1999-2001 ("3.2 Segmentation"), 2003, 2004-2005 (Table 1); Ex. 1003 ¶¶410-411. Thus, a POSITA would understand that the descriptions of "total number of segments" in Ex. 1014 corresponds to and discloses the "delivery cost term represents a segment count" recited claim 17. *See* Ex. 1003 ¶¶407-412.

Claim 17[a]: "…wherein simulated annealing is utilized to form the radiation therapy plan having a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost."

Webb 2001 in view of Shepard 2002 disclose the limitation of claim 17[a] "…***wherein simulated annealing is utilized to form the radiation therapy plan***…" as discussed below with respect to claim 20.

In addition, a POSITA would understand that it would be obvious to try for a POSITA regarding limitation "… [a] *radiation therapy plan having a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost*" as recited in claim 17. A POSITA would understand Shepard 2002 discloses the limitation "…[a] radiation therapy plan having a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost" recited in claim 17[a].

In addition, a POSITA would also be inclined to find claim 17[a] obvious to try the combination Webb 2002 in view of Shepard 2002. Shepard 2002 discloses using simulated annealing for optimization (Ex. 1010 1007 ("The leaf settings and the aperture intensities are optimized simultaneously using a simulated annealing algorithm.").) and allows a user to set limits on delivery values and explicitly states that its "technique allows the user to specify the maximum number of apertures per beam direction, and hence provides significant control over the complexity of the treatment delivery." . *Id*. ("A key feature of this approach is that the user specifies the number of segments to be delivered as a constraint in the optimization.")

Shepard 2002 uses the term "aperture" which a POSITA understands is being used as "opening(s)" which means "segment(s)" in the context of its "DAO" approach" *See* Ex. 1003 ¶¶418-419; Ex. 1010 1016 (Table III), 1017 (Table III).

TABLE III. A comparison of two treatment plans for a head and neck patient, one produced with direct aperture optimization, and one produced using CORVUS. In both cases, the same setup beam arrangement and treatment goals were used.

	Direct apertureoptimization	CORVUS
Total No. of segments	21	221
Total No. of monitor units	338	1761

Ex. 1010 (Table III)

Shepard 2002 also discloses "***having a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost***" as required by claim 17[a]. As explained in conjunction with Figure 16, Shepard 2002 states in the "E. Comparison with CORVUS" section that the Shepard 2002 solutions allows a delivery cost that does not exceed a predetermined segment count and has minimal dosimetric costs." Id. 1015 (Section E). As the two curves in the DVH shown in FIG. 16 illustrate, the DAO approach (solid line) has minimal dosimetric cost while not exceeding a predetermined segment count as opposed to the dashed line CORVUS optimized plan. *Id.* 1016.

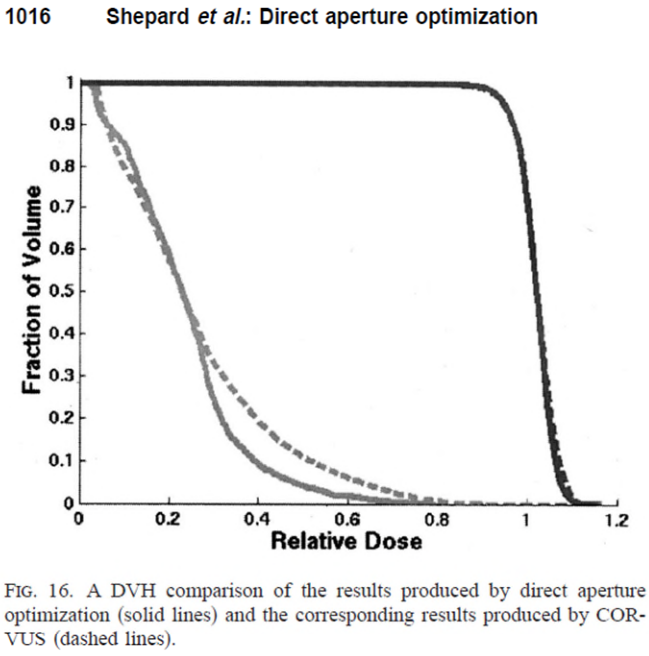


FIG. 16. A DVH comparison of the results produced by direct aperture optimization (solid lines) and the corresponding results produced by CORVUS (dashed lines).

Ex. 1010 (Figure 16)

Thus, in view of the teachings of Webb 2001 and Shepard 2002, a POSITA would know that it would be obvious to try and easily modify the "very simple

algorithm" of Webb 2001 to include a weighted beam factor measured by segments as taught in Shepard 2002 to allow a predetermined segment count to be entered by a user as a parameter and include a corresponding weighting factor "*w*" for that parameter given that Shepard 2002 discloses that a user may be afforded the ability to "specif[y] the number of segments" whereby "*a delivery cost not exceeding a predetermined segment count and having a minimal dosimetric cost*" may be achieved in a manner recited in claim 17[a]. Ex. 1003 ¶¶406-420. Thus, the combination of Webb 2001, Shepard 2002 and Bar 2001 render claim 17 obvious

XII. GROUND IV: WEBB 2001 IN VIEW OF BAR 2001, ALONE, OR IN FURTHER VIEW OF SIEBERS 2002 (CLAIM 8)

A. Claim 8. "A method as defined in claim 1. . ."

Claim 8 depends from claim 1. As discussed above in Section IX with regards to claim 1 and incorporated here, Webb 2001 discloses these claimed limitations. *See* Ex. 1003 ¶¶312-313.

Claim 8 [a]: "wherein delivery efficiency is represented by total monitor units to deliver the radiation treatment plan; and"

A POSITA would understand that Webb 2001 in further view of Siebers 2002 discloses claim 1[a] limitation. Webb 2001 reports that for treatment plans created by "[m]any inverse-planning algorithms and commercial systems," the dose space conformality is high but "the monitor-unit efficiency can be quite small, with unwanted consequences." *Ex. 1006.* N190 ¶1. "[M]onitor-unit efficiency"

includes any measure of the monitor units required for delivery of a treatment plan, such as the total number of monitor units required to deliver the treatment plan. Also, the second term in Webb 2001's hybrid cost function pertains to delivery costs. Ex. 1003 ¶315.

Siebers 2002 discloses "delivery efficiency [] represented by total monitor units to deliver the radiation treatment plan. . . "through its discussion of Table III and "number of monitor units." Ex. 1008 957 ¶4, 958 (Table III) ("The number of monitor units MUs required to deliver the deliverable treatment plans for each patient are summarized in Table III."); Ex. 1003 ¶316.

A POSITA would have reason to combine these teachings of Siebers 2002 with those of Webb 2001 because these references are very similar with both attempting to provide solutions to optimizing both conformity and delivery efficiency within the optimizer rather than in a separate step for leaf sequencing. *Id*. ¶317. both references discuss improving and controlling the degree of delivery efficiency of IMRT and recognize the advantage of affording a user control to select the degree of tradeoff between degree of conformity and delivery efficiency. *Id*.; *see* Ex. 1003 ¶¶313-316.

Claim 8 [b]: "wherein the step of providing control of a trade-off between treatment plan delivery efficiency and dosimetric fitness with an optimizer includes the step of limiting inflation of total monitor units from initially simple and efficient beam arrangements to more complex beam arrangements."

Claim 8[b] is disclosed by Ex. 1006 Webb 2001 in view of Ex. 1014 Bar 2001. Webb (2001) describes a cost function with "beam-space constraints," where "three weights w_1, w_2, w_3 control the relative contributions to the overall cost" by equation: $w_3[w_1 S_+ - w_2 F_{min}]$. Ex. 1006 N189 (Equation (2)). Ex. 1006 NN190; Ex. 1003 318-328.

Bar 2001 describes a sequencer "that can be integrated into any IMRT optimization algorithm," and which "allows the possibility of optimizing the sequencing with respect to the dose distribution. *See* Ex. 1014 Abstract, 1998 ¶2-3. As can be seen from Table 1 (shown in part below), Bar's results indicated that increasing the value of the bandwidth resulted in plans with a smaller number of segments. *Id.* Table 1.

Table 1. Analysis of the clustering and segmentation for 10 profiles with three different bandwidths. Listed are the resulting number of clusters and segments and rms and max for our clustering method (labelled with the subscript 1) and for the Bortfeld method (labelled as with the subscript 2). Bandwidth, rms and max have MU as their unit.

Profile	Bandwidth	Clusters	Segments	rms_1	rms_2	max_1	max_2
1	36.4	3	3	9.7	9.4	18.2	16.7
	18.2	4	4	6.7	7.1	11.4	12.5
	9.1	8	8	3.4	3.7	5.3	6.3
2	36.4	3	3	9.6	9.8	21.2	19.4
	18.2	5	4	5.4	6.1	10.9	11.8
	9.1	8	8	3.3	3.8	6.6	7.2
3	36.4	3	3	8.0	9.6	20.9	21.4
	18.2	4	4	5.9	7.0	14.0	14.3
	9.1	9	9	2.6	3.4	7.3	7.4

In addition, increasing the value of the bandwidth tended to result in higher "rms," which measures how different the clustered map is from the original fluence map—i.e. the dosimetric cost. Id.; Ex. 1003 ¶¶329-336 (reasons why a POSITA would combine Webb 2002, Bar 2002, Shepard 2002. Thus, the combination of Webb 2001 in view of Bar 2001, alone or in further view of Siebers 2002, renders claim 8 obvious.

XIII. GROUND V: WEBB 2001 IN VIEW OF BAR 2001, ALONE, OR IN FURTHER VIEW OF SIEBERS 2002, IN FURTHER VIEW OF SHEPARD (CLAIM 10, 19, 20)

A. Claim 10 (preamble). "A method as defined in claim 8…"

As discussed in Section XII regarding claim 8 and incorporated here, Webb 2001 in view of Siebers 2002 and Bar 2001 disclose this claimed limitation recited in the preamble of claim 10. Ex. 1003 ¶¶337-338.

Claim 10[a]: "wherein simulated annealing is utilized to form the radiation therapy plan with a substantially optimal dosimetric cost and a delivery cost not exceeding a predetermined total monitor units."

Claim 10[a] are the same as the limitations recited in claim 20 however, claim 10 depends from claim 8 (previously discussed) and claim 20 depends from claim 19. Shepard 2002 in view of Webb 2001 in view of Siebers 2002 and Bar 2001 (as discussed about with regards to the preamble and reference to claim 8) disclose claim 10[a]. Ex. 1003 ¶339.

Shepard 2002 discloses "*wherein simulated annealing is utilized to form the radiation therapy plan with substantially optimal dosimetric cost and a delivery cost not exceeding a predetermined total monitor units"* In Shepard 2002, simulated annealing is used in its DAO algorithm approach to form a radiation therapy plan, consistent with the limitations recited or that it would be obvious in view of the disclosure in Shepard 2002 to utilize simulated annealing to form a radiation therapy plan. *See e.g.*, Ex. 1010 Abstract: ("In this article, we introduce an automated planning system in which we bypass the traditional intensity optimization, and instead directly optimize the shapes and the weights of the apertures. We call this approach 'direct aperture optimization' [(DAO)]. . . The leaf settings and the aperture intensities are optimized simultaneously using a simulated annealing algorithm."); 1008 ("If the objective function value increases, the change is accepted with a probability P given by a standard Boltzmann

simulated annealing cooling schedule[13–15]"); 1010 (Fig. 6: "Fig. 6. A plot of the best objective function vs iteration. Note that with simulated annealing the current objective function both increases and decreases during the optimization"); 1013 ¶3 ("In Fig. 6, the objective function value for this case is plotted versus the iteration number. The change in objective function is less than 1% after 2000 iterations. Figure 6 plots both the current objective function value and the best objective function value. These two curves are not identical, because the simulated annealing algorithm will accept some changes that increase the objective function's value. At the end of the optimization, the optimizer outputs those settings" (emphasis added)); 1012 ¶4 (I. Consistence test "A key advantage of the use of a stochastic optimization approach such as simulated annealing is the ability to avoid local minima."); 1016 ¶2 ("Table III provides a comparison in terms of the number of segments and the total number of monitor units. The CORVUS plan used 221 segments as compared to 21 for the DAO plan. The CORVUS plan used 1761 MU as compared with 338 MU with the DAO plan. "); 1017 Table III (Table III: "TABLE III. A comparison of two treatment plans for a head and neck patient, one produced with direct aperture optimization, and one produced using CORVUS. In both cases, the same setup beam arrangement and treatment goals were used "); 1017 ("Another important feature of this tool [(i.e., DAO)] is the flexibility of simulated annealing algorithm.")

Further, the POSITA would further understand the description Shepard 2002 to also disclose the remaining portion of claim 10, ". . . ***substantially optimal dosimetric cost and a delivery cost not exceeding a predetermined total monitor units***." According Shepard 2002 "[t]his technique allows the user to specify the maximum number of apertures per beam direction, and hence provides significant control over the complexity of the treatment delivery." *Id.* Abstract. More specifically, as noted in the Abstract, the Shepard 2002 DOA algorithm/approach "can produce highly conformal step-and-shoot treatment plans using only three to five apertures per beam direction. As compared with traditional optimization strategies, our studies demonstrate that direct aperture optimization can result in a significant reduction in both the number of beam segments and the number of monitor units. Direct aperture optimization therefore produces highly efficient treatment deliveries that maintain the full dosimetric benefits of IMRT." Shepard 2002 1007 ("IV. Discussion" section); Ex. 1003 ¶¶339-364

B. Claim 19. "A method of providing control of a trade-off between treatment plan delivery efficiency and dosimetric fitness to optimize a radiation treatment plan within a continuum between delivery efficiency and dosimetric fitness, the method comprising the steps of…"

As discussed above in Section IX with regards to claims 1 (in particular claim 1[b] incorporated here, Ex. 1006 Webb 2001 discloses all of the limitations recited in the claim 19 preamble. *See* Ex. 1003 ¶422.

Claim 19 [a]: "evaluating an objective cost function within an optimizer for each of a plurality of intensity maps, the objective function including a dosimetric cost term and the delivery cost term and the delivery cost term representing total monitor units to deliver radiation according to a beam arrangement represented by the respective intensity map; and"

As discussed above in Section XII with regards to claim 8 incorporated here, Webb 2001 in view of Bar 2001 alone or in view of Bar 2001 further in view of Siebers 2002 discloses the claim 19[a]. *See Ex. 1003* ¶423.

Claim 19 [b]: "rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value."

Shepard 2002 discloses that its DAO approach uses simulated annealing. Ex. 1010 Abstract and 1017 ¶4 ("Another important feature of this tool is the flexibility of simulated annealing algorithm."). Shepard 2002 also discloses rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value using simulated annealing. *Id.* 1008 ("change in leaf position is rejected if the new aperture shape violates any of the constraints imposed by the multileaf collimator."); 1009 ("…one might choose to reject any change in leaf position that results in an aperture with an open area of less than 4 cm^2") Ex. 1003 ¶¶424-425. A POSITA knows that simulated annealing algorithms requires accepting or rejecting each intensity map as part of its technique and Shepard 2002 discloses using simulated annealing where "rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value …" is performed as

recited in claim 19[b]. Id. Thus, the combination of Webb 2001, Bar 2001 and Siebers 2002 render claim 19 obvious.

C. Claim 20. "A method as defined in claim 19 wherein simulated annealing is utilized to form the radiation therapy plan with substantially optimal dosimetric cost and a delivery cost not exceeding a predetermined total monitor units."

Claim 20 depends from claim 19. *See* Section XIII concerning claim 19 is incorporated here. Claim 20 is the same as the limitations recited in claim 10 however, claim 10 depends from claim 8 (previously discussed) and claim 20 depends from claim 19. Accordingly, the discussion of claim 10 hereby incorporated by reference here and for similar reasons as claim 10, Shepard 2002 in view of Webb 2001 in view of Siebers 2002 and Bar 2001 (as discussed about with regards to the preamble and reference to claim 19) disclose claim 20. Ex. 1003 ¶¶427-453.

XIV. GROUND VI: SHEPARD 2002 IN VIEW OF QUE 1999 (CLAIMS 11, 12)

A. Claim 11. "A method of providing control of a trade-off between treatment plan delivery efficiency and dosimetric fitness to optimize a radiation treatment plan within a continuum between delivery efficiency and dosimetric fitness, the method comprising the steps of…"

A POSITA would understand that Shepard 2002 and Que 1999 disclose all of the limitations recited in claim 11.

With respect to claim 11's preamble, a POSITA would understand that Shepard 2002 discloses the limitation recited in the preamble of claim 11.

Specifically, Shepard 2002 discloses a treatment planning approach in which the shape and weights of treatment segments are optimized directly and simultaneously, rather than addressing delivery constraints in a sequencing step after "traditional intensity optimization." In the described approach, the user is given control over the number of apertures per beam direction, and thus the complexity of the treatment plan, which allows the user to control the tradeoff between delivery efficiency and dosimetric fitness. *See* Ex. 1010 Abstract; 1017 ¶¶2-3 ("the user is given considerable control over the complexity of the treatment plan"); Ex. 1003 ¶¶365-371. Further, Shepard 2002 discloses "[t]he user specifies [treatment goals using a CDVH, including:] a minimum and a maximum dose for the tumor volume" and "for each sensitive structure, the user can specify the maximum dose allowed, a tolerance dose, and additional dose volume constraints" where "[t]he relative importance of each goal is input by the user as a numerical weight." *Id*. 1009 ¶2. From these paragraph of Shepard 2002, a POSITA would understand that the user is afforded control of the parameters associated with the treatment objectives, and hence the tradeoff between dosimetric fitness and treatment plan delivery efficiency, in a manner consistent with that recited in claim 11.

Claim 11 [a]: "applying prescription parameters to each of a plurality of optimization algorithms within an optimizer,"

A POSITA would recognize that Shepard 2002, or Shepard 2002 in view of Que 1999, discloses the step: "applying prescription parameters for each of a

plurality of optimization algorithms within an optimizer**.**" Shepard 2002 allows a user to specify minimum and maximum dose into an optimizer and specify the maximum number of beams, which can determine the type of optimization: Ex. 1010 at1009 ¶2; 1017 ¶¶2-3; Ex. 1003 ¶¶373-376.

In Que 1999, a similar recommendation is made regarding a plurality of algorithms: "it is desirable to have multiple algorithms available in a clinical treatment planning system, which will search through all algorithms automatically and find the most efficient delivery sequence for a given treatment. Each intensity map in a treatment could be delivered by a different algorithm, whichever is the most efficient for that map." Ex. 1012 Abstract, 2395 ¶4 (". . . an IMRT treatment planning system should implement multiple algorithms. . .") Given these descriptions concerning optimizing using multiple optimization algorithms, a POSITA art would understand that Shepard 2002 discloses all of the limitation of claim 11[a], or those limitations would be obvious to that person of ordinary skill when taken with Shepard 2002 in view of the Que 1999's recommendation. Ex. 1003 ¶¶372-378

Claim 11 [b]: "the plurality of optimization algorithms including a local optimization algorithm and a global optimization algorithm,"

Claim limitation 11[b] is also disclosed by Shepard 2002. A POSITA would understand Shepard 2002 to describe both local and global optimization algorithms amongst the plurality of possible optimization algorithms in the manner recited in

claim limitation 11[b]. A POSITA would understand that "simulated annealing" as discussed in Shepard 2002 is a "***global optimization algorithm***." Ex. 1010 Abstract ("…using a simulated annealing algorithm"); Fig. 6 and 1013¶3.

A POSITA would further understand that the "gradient-based optimization algorithms" discussed in Shepard 2002 are "***local optimization algorithms***." *Id.* 1012. ("A key advantage of the use of a stochastic optimization approach such as simulated annealing is the ability to avoid local minima.").

The POSITA would also understand that a particular treatment planning method may be implemented as either an iterative global optimization method or a local optimization method. *See, e.g., Id.* 1009 ¶6. Thus, Shepard 2002 discloses, or it would have been obvious to a POSITA in view of Shepard 2002, to have "***a plurality of optimization algorithms including a local optimization algorithm and a global optimization algorithm, the local optimization algorithm providing greater delivery efficiency than that of the global optimization algorithm, the global optimization algorithm providing greater dosimetric fitness than the local optimization algorithm.***" *Ex. 1003* ¶¶376-386.

Claim 11 [c]: "selecting one of the plurality of algorithms to be the optimizer responsive to a user selection between enhanced delivery efficiency and enhanced dosimetric fitness."

As discussed in the previous section, Shepard 2002 recognizes that selection between DAO and CORVUS algorithms could be done to achieve a selection

between enhanced delivery efficiency and enhanced dosimetric fitness as required by claim limitation 11[c]. *See* Ex. 1010 1015-1016 ¶1 ("In comparing the dose volume histograms, it can be *See*n that the plan produced using DAO provided improved tumor dose homogeneity as compared with CORVUS. The CORVUS plan, however, provided improved sparing of the critical structures. By adjusting the relative weights assigned to the treatment goals, it may be possible to further reduce the differences between these two plans."). A POSITA thus has the ability for selecting one algorithm from a plurality of algorithms "to be optimizer" (*sic*) based on the algorithm's relative delivery efficiency and dosimetric fitness compared to other algorithms.

Applying the teachings of Shepard 2002 with those of Exhibit 1012 (Que 1999) to achieve claim limitation 11 [c]. Que 1999 states:

> "no single algorithm is the most efficient for all clinical cases or intensity maps. This suggests that it is desirable to have multiple algorithms available in a clinical treatment planning system which will search through all algorithms automatically and find the most efficient delivery sequence for a given treatment. Each intensity map in a treatment could be delivered by a different algorithm, whichever is the most efficient for that map."

Ex. 1012 (Que 1999) Abstract. Que 1999 also recommends:

> By choosing algorithms carefully, it is possible to reduce the number of segments by a factor of 2 or more, while increasing the total monitor units by about 50% only. Our results suggest that ideally, an IMRT treatment planning system should implement multiple algorithms for MLC field segmentation.

> For each beam intensity map, the treatment planning software should search through different algorithms to find the delivery sequence with the least number of segments. . . . . This combined approach will be more efficient than using any single algorithm alone. Considering that IMRT treatment planning systems such as CORVUS generate hundreds of treatment plans before arriving at the final plan, this idea of generating many delivery sequences using different algorithms and then picking the best one seems very reasonable, and the additional computing time required is negligible.

Que 1999 2395 ¶¶3-4 (emphasis added). Que 1999 shows how the delivery efficiency of plans can be compared by tabulating the number of segments required for treatment plans generated by the different algorithms and parameters. *Id.* 2393-2394 (the results and legends for Tables I, II and III).

A POSITA one of ordinary skill in the art would take the recommendation of Que 1999 to characterize and select from a plurality of algorithms, where the selection is "*responsive to a user selection between enhanced delivery efficiency and enhanced dosimetric fitness,"* as described in Ex. 1010 Shepard 2001.

Ex. 1003 ¶¶387-392.

B. Claim 12."A method as defined in claim 11, wherein the global optimization algorithm is a simulated annealing algorithm, and wherein the local optimization algorithm is a gradient descent algorithm."

Claim 12 depends from claim 11. As discussed above in XIV.A and incorporated here, Shepard 2002 and Que 1999 disclose the claimed limitation.

Claim 12 [a]: "wherein the global optimization algorithm is a simulated annealing algorithm, and wherein the local optimization algorithm is a gradient descent algorithm."

Shepard 2002 discloses both global and local optimization algorithms in the manner recited in claim 12. Specifically, Shepard 2002 1009 ¶6 teaches a gradient based local optimization algorithm: "Within the context of our least squares objective function, DVH constraints are applied using a technique first described by Bortfeld et al.[18] for a gradient-based optimization algorithm and extended to an iterative format by Shepard et al.[19,20]".

Shepard 2002 also describes a simulated annealing global optimization algorithm in its Abstract, Fig. 6 and 1013 ¶3. *Id.* Abstract ("The leaf settings and the aperture intensities are optimized simultaneously using a simulated annealing algorithm"); *Id*. 1013 ¶3 ("Figure 6 plots both the current objective function value and the best objective function value. These two curves are not identical, because the simulated annealing algorithm will accept some changes that increase the objective function's value.")

Que 1999 also discloses simulated annealing-based global optimization algorithms and gradient decent based local optimization algorithms. In Tables 1, II, III of Que 1999 discusses simulated annealing-based global optimization algorithms and gradient decent based local optimization algorithms. Ex. 1012 Abstract, 2393-2394. Based on the discloses of Shepard 2002 and/or Que 1999, a

POSITA would understand that they both disclose algorithms where a simulated annealing algorithm is global optimization algorithms and a gradient descent algorithm is a local optimization algorithm as recited in claim 12.

A POSITA would also understand the take the recommendation of Que 1999 to characterize and select from a plurality of algorithms, where the selection is "*responsive to a user selection between enhanced delivery efficiency and enhanced dosimetric fitness,"* as described in Ex. 1010 Shepard 2001. Ex. 1003 ¶¶393-309.

XV. MOTIVATION TO COMBINE CITED REFERENCES

As discussed in the Seco Declaration (Ex. 1003 ¶¶196-22, 243-248), Ex. 1006 Webb 2001, Ex. 1008 Siebers 2002 and Ex. 1014 Bar describe methods for IMRT optimization, specifically, MLC leaf optimization techniques as of the '175 patent's earliest effective date. Bar 2001 describes a step and shoot sequencer that "can be integrated into an IMRT optimization algorithm." *See* Bar 2001 Abstract.

Ex. 1006 Webb 2001 discloses that you get a better radiation therapy treatment plan if you include both a dosimetric term and a delivery term in your objective function and describes "a tradeoff between obtaining desirable features in beam-space and high conformality in dose-space." Ex. 1006 Abstract. Webb 2001 further discloses the "tradeoff "can be under the control of the user." *Id.* N190.

Ex. 1006 Webb 2001 is referenced by Exhibit 1008 Siebers 2002. Ex. 1008 959. Exhibit 1008 Siebers also discloses that "Webb [2001] included cost functions

that took into account the ‘‘complexity’’ of the intensity profiles in IMRT optimization, thus encouraging the optimizer to find less complex solutions when performing the beamlet intensity optimization.” *Id.* 953.

Ex. 1014 Bar 2001 discloses that “[a]dvantages of the step and shoot method are the relative ease of quality assurance and its close relationship with conventional conformal therapy.” Bar 2001 1997. “[W]e describe a step and shoot sequencer that can be integrated into the optimization process of our treatment planning program. It considers all technical limitations of the MLC.” *Id.* 1998. Bar is designed to be integrated into the optimization process of Webb 2001 and Ex. 1008 Siebers 2002.

A POSITA searching for articles related to “tradeoff, or correlation, between the factors of treatment plan efficiency and dosimetric fitness to optimize a radiation therapy,” would have considered Webb 2001, Bar 2001 and Ex.1008 Siebers 2002.

Further, as discussed in the Ex. 1003 Seco Declaration (¶¶249-255), Ex. 1008 Shepard 2002 and Que 1999 describe methods for IMRT optimization, specifically, MLC leaf optimization techniques as of the ’175 patent’s earliest effective date.

Ex. 1010 Shepard 2002 discloses a comparison of DAO with NOMOS CORVUS and notes that DAO reduces monitor units and segments, which a user

can tweak to make them even closer (i.e. emphasize dosimetric fitness). *See* Ex. 1010 1015. Ex. 1010 Shepard 2002 also references Ex. 1030 Dai 2001 (discussed above). Ex. 1015 1014.

Ex. 1030 Dai 2001 references Que 1999 and its author "thank[ed] Dr. William Que for provision of the prostate case and for helpful discussions on this paper." Ex. 1030 2120; Ex. 1003 ¶254.

In view of the above, a POSITA searching for articles related to "tradeoff, or correlation, between the factors of treatment plan efficiency and dosimetric fitness to optimize a radiation therapy," would have considered Shepard 2002 and Que 1999.

XVI. SECONDARY CONSIDERATIONS OF NON-OBVIOUSNESS DO NOT NEGATE OBVIOUSNESS

Petitioner is not aware of any secondary considerations that would demonstrate non-obviousness in view of the art relied on in this Petition. Moreover, a strong showing of obviousness, as here, overcomes secondary considerations. *See*, e.g., *Leapfrog Enters, Inc*. v. *Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (2007); *Dow Chemical Co.* v. *Halliburton Oil Well Cementing Co.*, 324 U.S. 320, 330 (1945) ("[Secondary] considerations are relevant only in a close case.").

Petitioner also is not aware of any nexus between any alleged commercial success and "the merits of the claimed invention." *Ohio Willow Wood Co*. v. *Alps South, LLC*, 735 F.3d 1333, 1344 (2013); *Wyers* v. *Master Lock Co*., 616 F.3d 1231, 1246 (2010) ("[f]or objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention.)

It is Patent Owner's burden of production to provide evidence of secondary considerations. *Medtronic Inc.* v. *NuVasive Inc*., IPR2014-00087, Paper 44 21 (PTAB Apr. 3, 2015). Petitioner reserves the right to provide a full rebuttal to any secondary consideration evidence provided during this proceeding.

Petitioner reserves the right to provide a full rebuttal to any secondary consideration evidence provided during this proceeding. Petitioner cannot address such evidence in sufficient depth now because Patent Owner has not yet provided any.

Petitioner notes, however, that "[f]or objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *Wyers* v. *Master Lock Co*., 616 F.3d 1231, 1246 (2010). Moreover, a strong showing of

obviousness, as in this case, overcomes secondary considerations. *See*, e.g., *Leapfrog Enters, Inc*. v. *Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (2007).

Petition further notes that the Patent Owner may *See*k to introduce evidence of secondary considerations. But secondary considerations do not establish that the proposed combinations and modifications would not have been obvious to one of ordinary skill in the art. First, as explained in Sections IX and X Petitioner has shown a strong case of obviousness, which cannot be overcome with secondary considerations. *Dow Chemical Co.* v. *Halliburton Oil Well Cementing Co.*, 324 U.S. 320, 330 (1945) ("[Secondary] considerations are relevant only in a close case."). Second, it is Patent Owner's burden of production to provide evidence of secondary considerations. *Medtronic Inc.* v. *NuVasive Inc.*, IPR2014-00087, Paper 44 21 (PTAB Apr. 3, 2015).

Finally, Petitioner notes that they are not aware of any evidence of commercial success for the system disclosed in the '175 patent that would show the claimed system was non-obvious. Further, there is no nexus between any alleged commercial success and "the merits of the claimed invention." *Ohio Willow Wood Co*. v. *Alps South, LLC*, 735 F.3d 1333, 1344 (2013), particularly since the only elements that even the Patentee asserted were novel during prosecution are "giving the user the ability to control directly on a patient-by-patient basis the competing needs of

conformality/avoidance (dosimetric fitness) and efficiency," by "adding a delivery cost term in the cost function that quantifies plan efficiency." Ex. 1003 ¶¶255-260.

XVII. CONCLUSION

For the reasons set forth above, Elekta requests that the Board institute *IPR* of and cancel the Challenged Claims.

Dated: October 18, 2019

/Tamara D. Fraizer #51669/

TAMARA D. FRAIZER
Squire Patton Boggs (US) LLP
1801 Page Mill Road, Suite 110
Palo Alto, CA 94304-1043
Telephone: (650) 843-3201
Facsimile: (650) 843-8777
Email: tamara.frazier@squirepb.com
Registration No.: 51669

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Petition for *Inter Partes* Review of U.S. Patent No. 7,266,175 contains, as measured by the word-processing system used to prepare this paper, 13,884 words. This word count does not include the items excluded by 37 C.F.R. § 42.24 as not counting towards the word limit.

Dated: October 18, 2019

/Tamara D. Fraizer #51669/

TAMARA D. FRAIZER
Squire Patton Boggs (US) LLP
1801 Page Mill Road, Suite 110
Palo Alto, CA 94304-1043
Telephone: (650) 843-3201
Facsimile: (650) 843-8777
Email: tamara.frazier@squirepb.com

Registration No.: 51,699

CERTIFICATE OF SERVICE

The undersigned certifies pursuant to 37 C.F.R. § 42.6(e) and § 42.105 that on October 21, 2019 a true and correct copy of the foregoing will be served via USPS Express Mail Federal Express on the Patent Owner at the following correspondence address of record as listed on PAIR:

Buchanan Ingersoll & Rooney, PC
P.O. Box 1404
Alexandria, VA 22313-1404

and was served via electronic mail upon counsel of record for the Patent Owner in the litigation pending before the U.S. District Court for the Northern District of Georgia entitled *Best Medical International, Inc., v. Elekta Inc. and Elekta Limited*, Case No. 1:19-cv-03409.

Anand Mohan Erin M. Dunston Buchanan Ingersoll & Rooney, PC Suite 500 1737 King Street Alexandria, VA 22314-2727 anand.mohan@bipc.com erin.dunston@bipc.com	Jason P. Camillo Buchanan Ingersoll-Pittsburg 301 Grant Street One Oxford Centre, 20th Floor Pittsburgh, PA 15219 jason.camillo@bipc.com
Philip L. Hirschhorn Jennifer Liu Buchanan Ingersoll & Rooney, PC 9th Floor 640 Fifth Avenue New York, NY 10019 philip.hirschhorn@bipc.com jennifer.liu@bipc.com	John Weldon Harbin Meunier Carlin & Curfman, LLC Suite 1300 999 Peachtree Street NE Atlanta, GA 30309 jharbin@mcciplaw.com

Dated: October 18, 2019

/Tamara D. Fraizer #51669/
TAMARA D. FRAIZER
Squire Patton Boggs (US) LLP
1801 Page Mill Road, Suite 110
Palo Alto, CA 94304-1043
Telephone: (650) 843-3201
Facsimile: (650) 843-8777
Email: tamara.frazier@squirepb.com

Registration No.: 51,699