UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

VARIAN MEDICAL SYSTEMS, INC.,
Petitioners

v.

BEST MEDICAL INTERNATIONAL, INC.,
Patent Owner

Case IPR2020-00053
U.S. Patent No. 7,266,175
Issue Date: September 4, 2007

Title: PLANNING METHOD FOR RADIATION THERAPY

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

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List of Exhibits

Exhibit No.	Description of Document
1001	U.S. Patent No. 7,266,175 B1 to Merle Romesberg (filed July 9, 2004, issued September 4, 2007) ("'175" or "'175 patent")
1002	Declaration of Timothy D. Solberg, Ph.D. ("Solberg")
1003	"A Simple Method to Control Aspects of Fluence Modulation in IMRT Planning," *Physics in Medicine & Biology,* 46:N187-N195 (2001) ("Webb 2001")
1004	"The Impact of Fluctuations in Intensity Patterns on the Number of Monitor Units and the Quality and Accuracy of Intensity Modulated Radiotherapy," *Medical Physics*, 27(6):1226-1237 (2000) ("Mohan")
1005	*The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning* (1993) ("Webb 1993")
1006	"Incorporating multi-leaf collimator leaf sequencing into iterative IMRT optimization," *Medical Physics*, 29(6):952-959 (June 2002) ("Siebers")
1007	Amendment and Response to Office Action Dated October 25, 2006 filed in U.S. Appl. 10/887,966 ("01/30/2007 Response")
1008	Amendment and Response to Office Action Dated May 3, 2006 filed in U.S. Appl. 10/887,966 dated August 7, 2006 ("08/07/2006 Response")
1009	Declaration of Mark P. Carol submitted re U.S. Appl. No. 10/887,966, dated January 2007 ("Carol Decl.")
1010	U.S. Patent 6,393,096 to Mark P. Carol et al. (filed May 27, 1999, issued May 21, 2002)
1011	Declaration of Sylvia Hall-Ellis, Ph.D.

Exhibit No.	**Description of Document**
1012	U.S. Patent 6,038,283 to Mark P. Carol et al. (filed October 24, 1997, issued March 14, 2000)
1013	"IMRT: Where We Are Today," *The Theory and Practice of Intensity Modulated Radiation Therapy* (1997) ("Carol Textbook")
1014	"Optimization of conformal radiotherapy dose distributions by simulated annealing: 2. Inclusion of scatter in the 2D technique," S. Webb ("Webb 1991")
1015	"Optimisation of conformal radiotherapy dose distributions by simulated annealing," S. Webb ("Webb 1989")

Petitioner Varian Medical Systems, Inc. ("Petitioner") respectfully submits this Petition for Inter Partes Review of claims 13-16, 18, and 19 of U.S. Patent No. 7,266,175 [Ex. 1001] ("the '175 patent").

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

A. Real Party-In-Interest Under 37 C.F.R. §42.8.(b)(1)

In addition to Petitioner Varian Medical Systems, Inc., VMS International AG and its two Dutch parent companies, VMS International Holdings, Inc., VMS Netherlands Holdings, Inc., and VMS Nederland BV are real parties-in-interest.

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

The '175 patent is the subject of one pending litigation involving Petitioner: *Best Medical International, Inc. v. Varian Medical Systems, Inc.*, Case No. 1:18-cv-01599-UNA (D. Del. Oct. 16, 2018). Petitioner was served with a complaint in that action on October 18, 2018.

Petitioner is unaware of any previous petition for *inter partes* review of the '175 patent.

C. Lead and Back-Up Counsel under 37 C.F.R. §42.8(b)(3)

Petitioner provides the following designation of counsel.

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D. Service Information

This Petition is being served by Federal Express to the attorney of record for the ’175 patent, Best Medical International, Inc., Patent Counsel, 7643 Fullerton Road, Springfield, VA 22153. Petitioner consents to electronic service at the addresses provided above for lead and back-up counsel.

II. FEE PAYMENT

Petitioner requests review of six claims, with a $30,500 payment.

III. REQUIREMENTS UNDER 37 C.F.R. §§ 42.104 AND 42.108

A. Grounds for Standing

Petitioner certifies that the ’175 patent is available for IPR and that Petitioner is not barred or otherwise estopped.

B. Identification of Challenge and Statement of Precise Relief Requested

The Petitioner requests institution of IPR based on:

Ground	Claims	Basis for Challenge under §103(a)
1	13-15	Webb 2001 (Ex. 1003), Mohan (Ex. 1004)
2	16, 18, 19	Webb 2001, Mohan, Webb 1993 (Ex. 1005)
3	13-15	Webb 2001, Mohan, Siebers (Ex. 1006)

Ground	Claims	Basis for Challenge under §103(a)
4	16, 18, 19	Webb 2001, Mohan, Webb 1993, Siebers

Submitted with this Petition is the Declaration of Dr. Timothy Solberg (Ex. 1002), a qualified expert. (Solberg, ¶¶1-8, Ex. A.)

IV. LEVEL OF ORDINARY SKILL IN THE ART

A person of ordinary skill as of July 2003 would be a medical physicist with a Ph.D. (or similar advanced degree) in physics, medical physics, or a related field, and two or more years of experience in radiation oncology physics treatment planning, treatment plan optimization related to radiation oncology applications, and computer programming associated with treatment plan optimization (or equivalent degree or experience). (Solberg, ¶13.)

V. TECHNOLOGY BACKGROUND

Dr. Solberg has provided an overview of the technology relevant to the ’175 patent, reproduced in condensed form below. (Solberg, ¶¶24-32.)

A. Intensity Modulated Radiation Therapy (IMRT)

An intensity modulated radiation therapy (IMRT) treatment plan typically employs multiple treatment beams or “fields,” and the intensity of each beam or field is further “modulated” within the beam itself – hence the term “*intensity modulated* radiation therapy.” (Solberg, ¶¶24-26.) To that end, each beam is further divided into smaller “beamlets,” and the radiation intensity of each beamlet is specified during treatment planning by a corresponding "beam weight" assigned to that beamlet. (Solberg, ¶27.) This is shown in the following figure from a textbook chapter on IMRT authored by Mark P. Carol (a former employee of NOMOS, the assignee appearing on the face of the '175 patent):

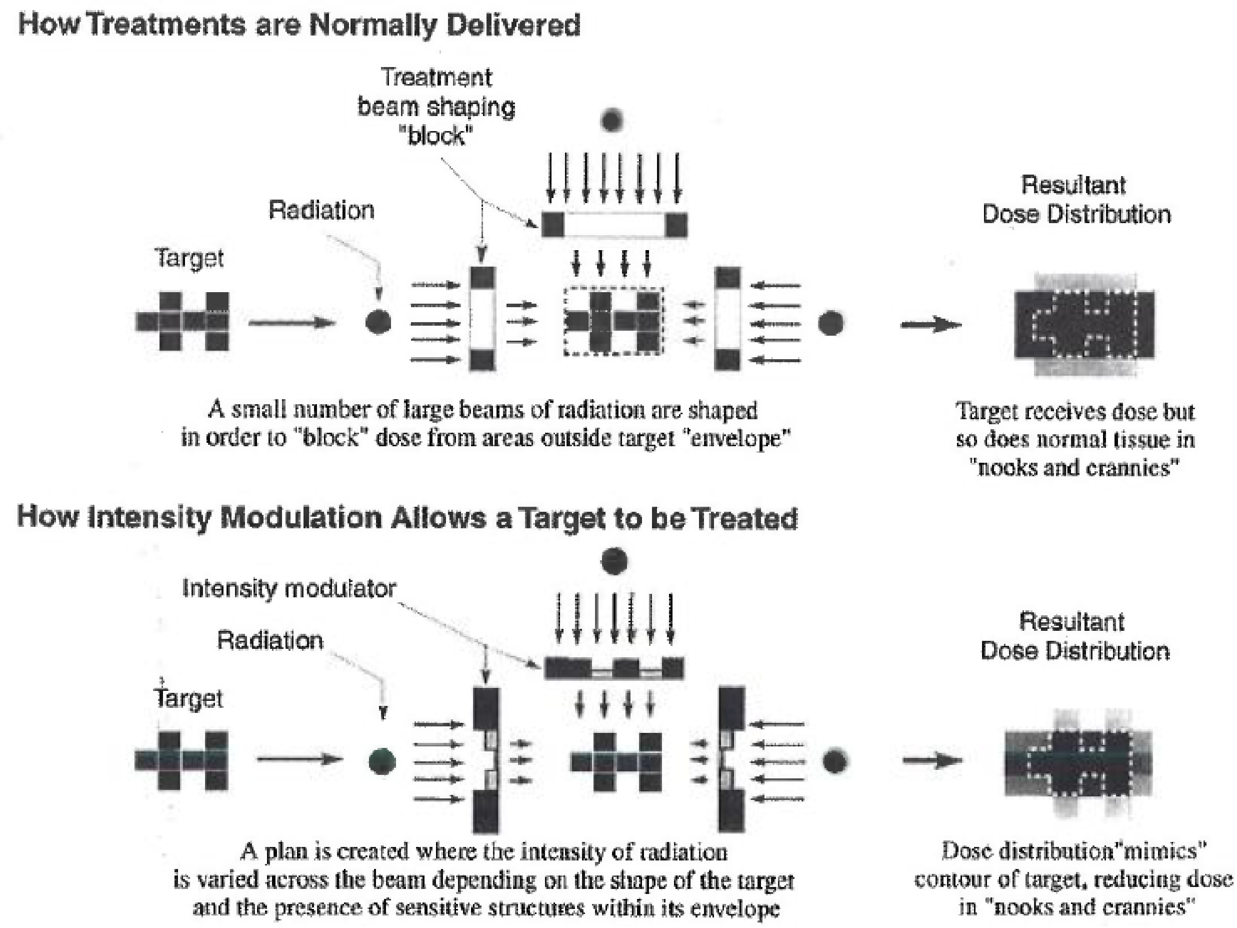


Figure 1. Conventional versus IMRT delivery.

(Solberg, ¶27 (citing Ex. 1013).)

The bottom half of the figure shows a simplified hypothetical treatment plan that uses three beams, and the radiation intensity is further varied or "modulated" within each beam. The intensity modulated radiation delivered by the three beams combine to create the resultant "dose distribution" at the target site, shown above at bottom right.

B. Treatment Planning and the Use of Cost Functions

The "beam weights" that specify the respective intensities of beamlets within each beam of the multi-beam arrangement, as discussed above, are generated through a computer-based treatment planning process. (Solberg, ¶¶28-29.) One form of treatment planning uses an "iterative" technique, which proceeds by randomly changing beam weights and then evaluating the effect of each change on the dose distribution. (Solberg, ¶30.) The evaluation of each change to the beam weights uses what is known as a "cost function" (sometimes referred to as an "objective" function), in which solutions with a lower cost are viewed as being more desirable than solutions with a higher cost. (*Id.*)

The aim of the treatment planning optimization process is to minimize the cost function. (Solberg, ¶31 (citing Ex. 1005).) To provide an example, a well-known type of cost function calculates the difference between the prescribed dose distribution and the dose distribution that would result from the multi-beam arrangement specified by the beam weights being evaluated at a given iteration of the optimization process. (Solberg, ¶32.) In this example, a minimized value for the cost function would correspond to a minimal difference between the prescribed dose distribution and the dose distribution that would be delivered by the treatment plan. This example thus illustrates how the cost function drives the optimization process towards the desired outcome.

VI. SUMMARY OF THE ’175 PATENT

The ’175 patent is entitled “Planning Method for Radiation Therapy,” and purports to provide a “[m]ethod and apparatus for controlling the correlation between the factors of treatment plan efficiency and dosimetric fitness” to optimize a radiotherapy plan. (’175, Abstract.) In its “Background of the Invention” section, the ’175 patent explains that “[t]raditional inverse intensity modulated radiation therapy (‘IMRT’) planning systems attempt to find radiation intensity maps resulting in the best calculated dose distribution for a specific tumor for a specific patient” using, “typically, a conventional linear accelerator provided with a multileaf, or multiple leaf, collimator (‘MLC’).” (’175, 1:13-20.)

The ’175 patent further explains:

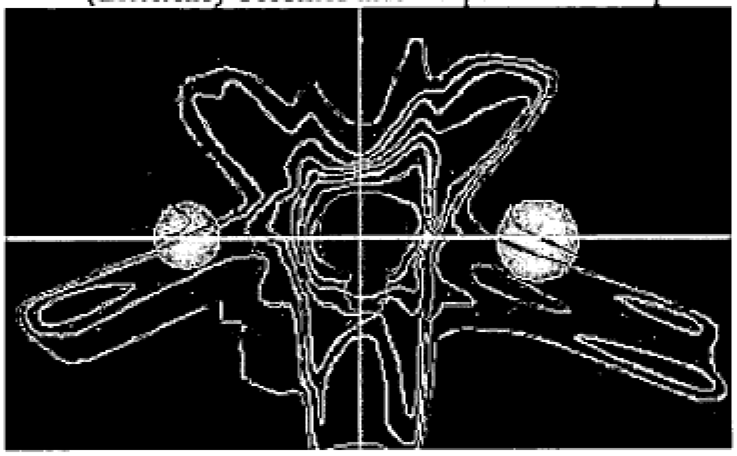
> For many treatment plans, the resultant intensity maps often cannot be efficiently delivered by the radiation therapy treatment equipment…. Inefficient intensity maps may require a large number of monitor units (“MU”) or a large number of “MLC” segments for delivery. These inefficient treatment plans, or solutions, are undesirable because they might require a large amount of delivery time, radiation beam on time, and/or radiation leakage dose to the patient. It is also undesirable to

> uniformly preclude the discovery of less efficient treatment plans, which may also be dosimetrically superior plans. Thus, it would be desirable to provide 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.

('175, 1:16-32.)

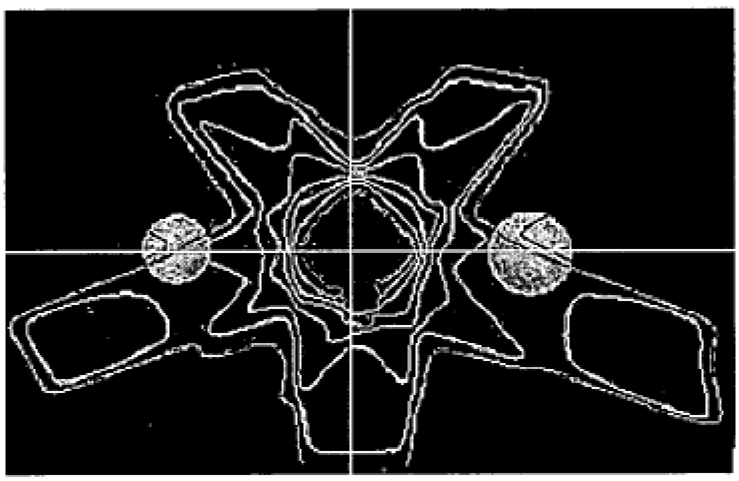
The tradeoff between dosimetric fitness and delivery efficiency in treatment plans is illustrated in the "dose distribution intensity maps" shown in Figures 2A-2C and 4A-4C:

(Efficiency becomes more important from top to bottom):



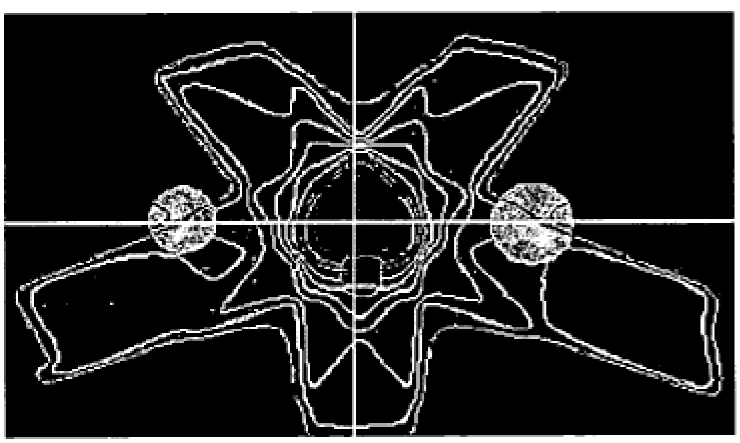
Dosimetric Cost = 0.453
Segment Count = 97

FIG. 2A.



Dosimetric Cost = 0.653
Segment Count = 37

FIG. 2B.

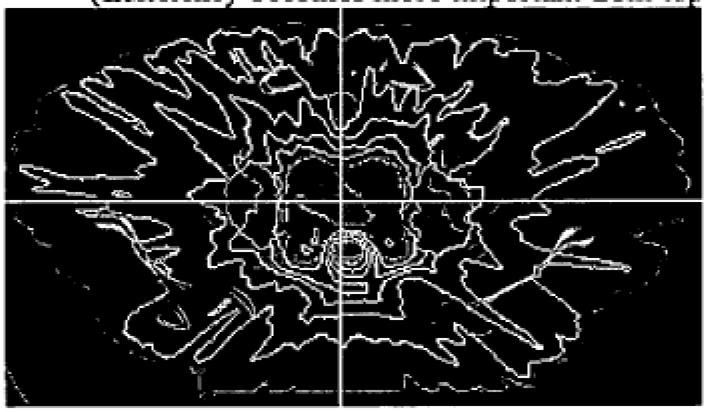


Dosimetric Cost = 1.26
Segment Count = 5

FIG. 2C.

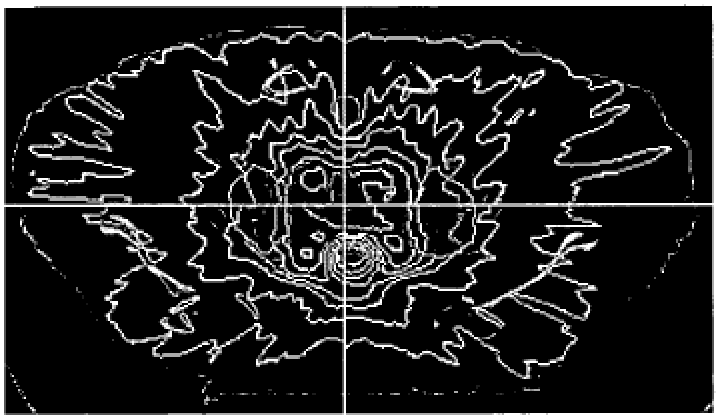
('175, Figs. 2A-2C; *see also id.*, 1:66-67 ("FIGS. 2A-2C are dose distribution intensity maps for three different radiotherapy plans;").)

(Efficiency becomes more important from top to bottom):



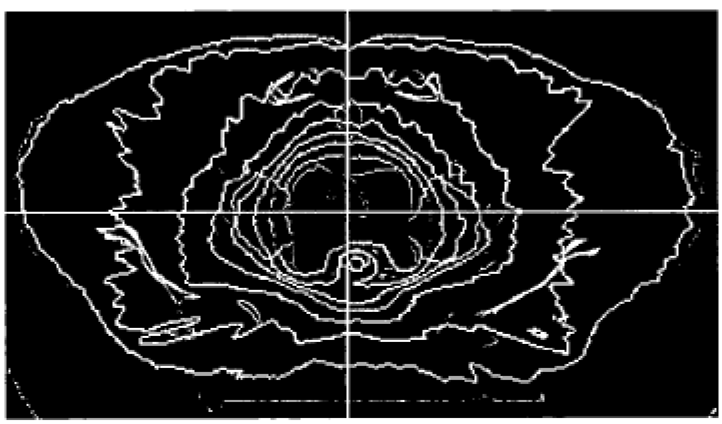
Dosimetric Cost = 0.132
Total Monitor Units = 22365

FIG. 4A.



Dosimetric Cost = 0.149
Total Monitor Units = 15624

FIG. 4B.



Dosimetric Cost = 1.94
Total Monitor Units = 6640

FIG. 4C.

(*Id.*, Figs. 4A-4C; *see also id.*, 2:3-4 ("FIGS. 4A-4C are dose distribution intensity maps for three different radiotherapy plans;").)

"FIGS. 2A-2C illustrate the tradeoff, or correlation, between Segment Count and Delivery Efficiency, and Dosimetric Cost, on a clinical treatment plan. As the Segment Count is decreased, the dose distribution becomes less conformal as the Dosimetric Cost increases. Thus, Delivery Efficiency although higher for FIG. 2C, has a poorer Dosimetric Fitness." ('175, 3:31-37.) Likewise, "FIGS. 4A-4C illustrate the tradeoff on a clinical treatment plan. As the Total Monitor Units are decreased, as shown going from FIG. 4A to FIG. 4C, the dose distribution becomes less conformal, or desirable, as the Dosimetric Cost increases. Thus, Delivery Efficiency, although higher for FIG. 4C, has a poorer Dosimetric Fitness." ('175, 3:50-55.)

The '175 patent states that a user can control the tradeoff between dosimetric fitness and delivery efficiency, by controlling the number of MLC segments in a treatment plan and similarly, controlling the number of monitor units (MUs). ('175, 1:36-47.)[1] As noted in the '175 patent, the number of monitor units is proportional to the radiation "beam on" time. ('175, 2:28-35.)

VII. CLAIM CONSTRUCTION

A claim term must be construed "[i]f a petitioner believes that a claim term requires an express construction." (Office Patent Trial Practice Guide, July 2019

[1] All underlining, italics, and annotations has been added by Petitioner unless noted otherwise.

Update at 13.) "On the other hand, a petitioner may include a statement that the claim terms require no express construction." (*Id.*)

For purposes of this Petition, Petitioner identifies the following terms.[2] For claim terms not identified, Petitioner has applied the plain and ordinary meaning of those terms.

A. "optimizer"

The term "**optimizer**" appears in a number of claims of the '175 patent. For example, independent claim 11 recites "selecting one of the plurality of algorithms to be the optimizer." ('175, 5:64-65.) Consistent with how the term is used in claim 11, an "**optimizer**" would have been understood by persons of ordinary skill in the context of the '175 patent to refer to a form of an **algorithm** used for treatment planning. (Solberg, ¶40.)

The Applicant during prosecution further provided the following explanation on the operation of an "**optimizer**":

> [T]he delivery cost term is not a term quantified directly by the clinician

[2] The initial exchange of claim terms and proposed constructions in the underlying litigation is due November 22, 2019. Per the district court's order, the parties are to subsequently meet and confer and prepare a joint claim construction chart on December 20, 2019, followed by briefing in January through March of 2020.

> to allow the clinician to determine how fast the plan can be delivered, but 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*."

(Ex. 1007, 01/30/2007 Response, at 9; *see also* Ex. 1008, 08/07/2006 Response (similar), at 12; Ex. 1009, Carol Decl. at 4, ¶6a5 (similar).)

An "**optimizer**" is thus also an **iterative** process, as the above passage makes clear. The passage's description of an "**optimizer**" as involving the use of a "delivery cost term" and an "objective function" is consistent with the recitation of an "**optimizer**" in claims 13 and 19. Claim 13 recites "assigning a delivery cost term within an optimizer." Claim 19 likewise recites "evaluating an objective cost function within an optimizer."

Accordingly, the term "**optimizer**" should be interpreted to mean an "**iterative optimization algorithm**." This interpretation is further supported by the patent specification, which describes the optimizer as "progress[ing]" through multiple potential treatment plans:

> A second method for providing user control in a treatment plan provides user control of total monitor units. The acceptable inflation, or increase, of total monitor units is limited as the optimizer *progresses* from

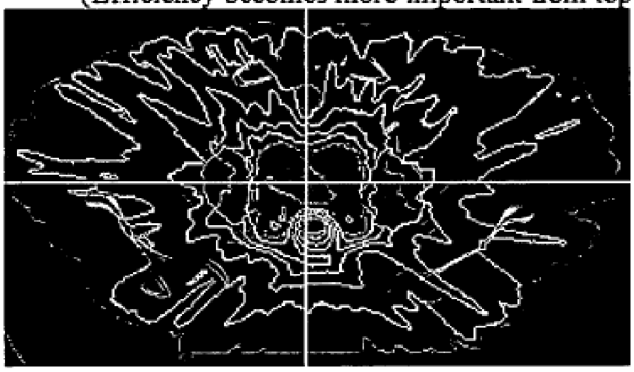
simple, efficient treatment plans toward more complex treatment plans.

('175, 1:42-47.)

B. "intensity map"

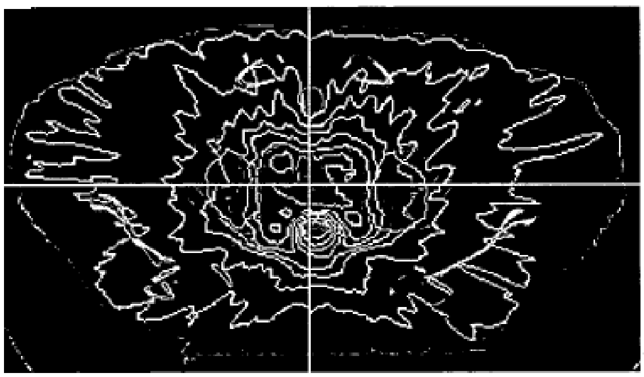
As explained by Dr. Solberg, the term "**intensity map**" in intensity modulated radiation therapy ("IMRT") typically refers to the intensity or "fluence" profile of a *single* radiation beam in a multi-beam arrangement. (Solberg, ¶¶44-45 (citing Ex. 1013).) In the traditional context, an intensity map is used to describe properties of a single beam, but obviously cannot provide information about the dosimetric fitness of the dose distribution of all beams. But the '175 patent uses "**intensity map**" in a different way. The '175 patent purports to show "dose distribution intensity maps" in Figures 2A-2C, 4A-4C, 7, and 8. ('175, 1:66-67, 2:3-4, 2:10-11, 2:11-12.) Some of these figures are reproduced below:

(Efficiency becomes more important from top to bottom):



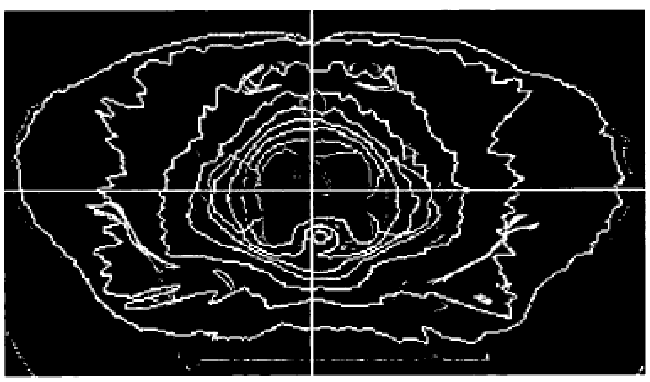
Dosimetric Cost = 0.132
Total Monitor Units = 22365

FIG. 4A.



Dosimetric Cost = 0.149
Total Monitor Units = 15624

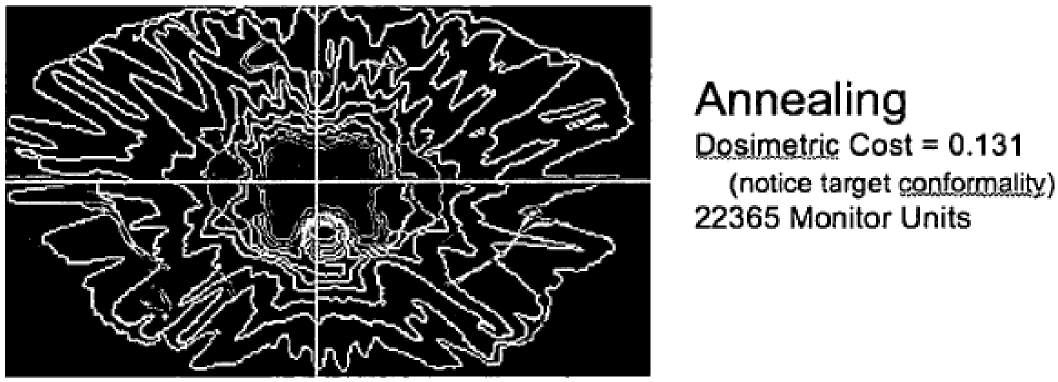
FIG. 4B.



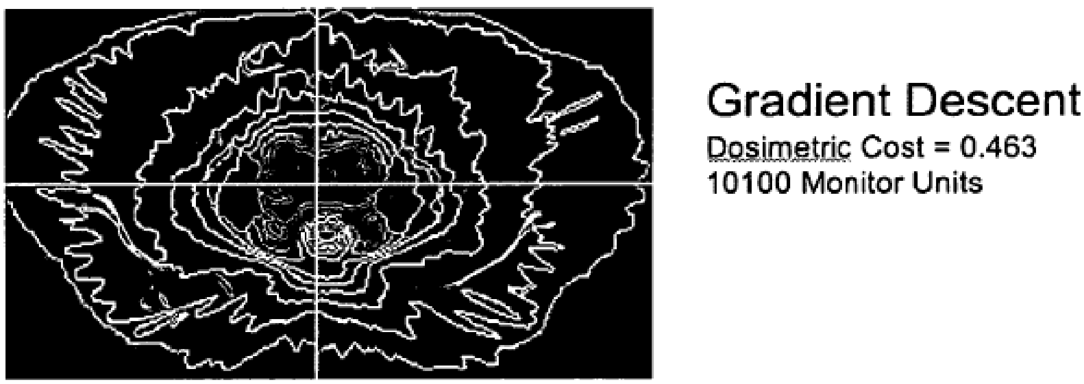
Dosimetric Cost = 1.94
Total Monitor Units = 6640

FIG. 4C.

('175, Figs. 4A-4C.)



(’175, Fig. 7.)



(’175, Fig. 8.)[3]

Contrary to typical usage, in which an “**intensity map**” represents the *intensity profile* of a *single beam*, an “**intensity map**” as used in the ’175 patent represents the resultant *dose distribution* created by *multiple beams* positioned

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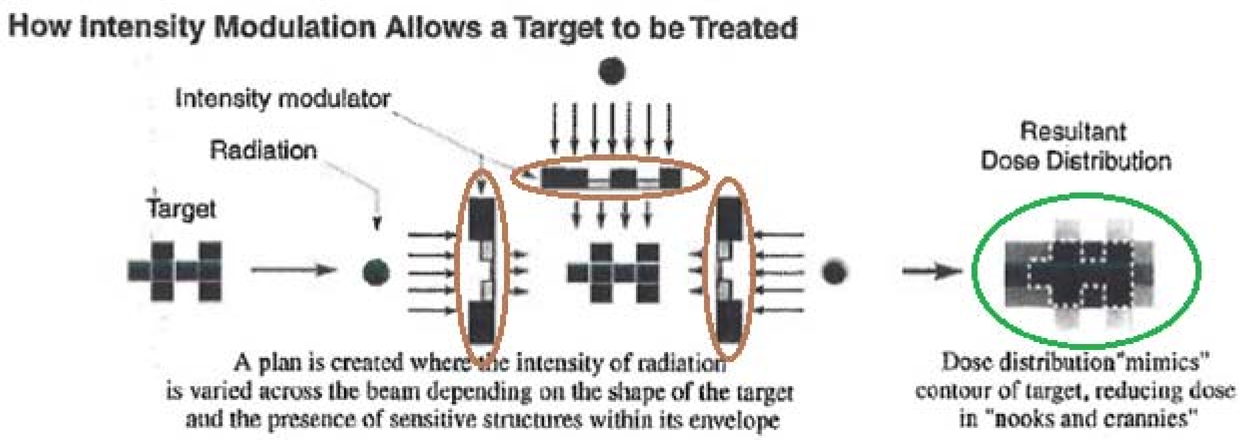
[3] As explained by Dr. Solberg, the jagged lines shown are known as “isodose” lines, and each line traces through locations that all have the same dose, hence the term “iso” dose. (Solberg, ¶48 n.1.)

around the target. (Solberg, ¶¶47-48.) This can be readily appreciated by comparing the above figures from the '175 patent to the figure below, taken from a textbook chapter written by Carol:



(Ex. 1013 at 19 (Fig. 1) (partial figure).)

Therefore, consistent with the figures showing "dose distribution intensity maps" provided in the '175 patent, and the detailed description of use of intensity maps to evaluate dosimetric fitness of a treatment plan, the term "**intensity map**" should be construed to mean a "**representation of dose distribution**." As the Federal Circuit has explained, "a claim term may be clearly redefined without an explicit statement of redefinition and even when guidance is not provided in explicit definitional format, the specification may define claim terms by implication such that the meaning may be found in or ascertained by a reading of the patent documents." *Trustees of Columbia Univ. v. Symantec Corp.*, 811 F.3d 1359, 1364 (Fed. Cir. 2016) (brackets, quotation marks and citation omitted).

This construction is further supported by the patent claims. For example, independent claim 13 recites "evaluating an objective cost function for each of the plurality of intensity maps, the objective function including a dosimetric cost term… the dosimetric cost term representing dosimetric fitness of the respective intensity map."[4] This limitation would be rendered nonsensical if the "respective **intensity map**," as claimed, represents a single beam rather than the entirety of a multi-beam arrangement. (Solberg, ¶50.) This is because the recited "dosimetric fitness" and "dosimetric cost" refer, respectively, to the fitness and quantified cost of a *dose distribution*, as the '175 specification itself makes clear:

> Dosimetric Fitness may be quantified with reference to "Dosimetric Cost." For Dosimetric Cost in an inverse IMRT treatment planning system, the ***fitness*** of a ***dose distribution*** is typically quantified by using

[4] Other claims recite similar limitations. For example, independent claim 1 recites "evaluating a cost function for each of a set of a plurality of candidate intensity maps… the cost function including a dosimetric cost term representing dosimetric cost and related to dosimetric fitness of the respective candidate intensity map." Similarly, independent claim 19 recites "evaluating an objective cost function… for each of a plurality of intensity maps, the objective function including a dosimetric cost term."

> a dosimetric cost function. ***Dose distributions*** with low ***Dosimetric Cost*** are generally deemed superior to those with a high Dosimetric Cost.

('175, 2:40-45; *see also* Ex. 1008, 08/07/2006 Response, at 12.) And a "dose distribution" – and likewise its corresponding "fitness" and cost" – cannot be evaluated based on any single beam alone. (Solberg, ¶51.) Rather, as explained in U.S. Patent 6,393,096, incorporated by reference into the '175 patent ('175, 4:27-32), dose depends on "[t]he cumulative effect of multiple beams passing through the treatment field":

> [I]f a single beam is used, the beam weight, or intensity, at the epicenter 602 would be 78% of the dose at the entrance point 603. If a second beam of equal intensity were directed toward the treatment field from the direction indicated by arrow 610 (FIG. 6B) and placed so that the two beams intersected only at the epicenter 602, the dose at the epicenter 602 would be two times 78%, or 156% of the dose from each respective treatment beam. The cumulative effect of multiple beams passing through the treatment field from the different entrance paths 600, 610 thereby creates a concentration of dose to occur at the epicenter 602.

(Ex. 1010, U.S. Patent 6,393,096, 5:28-38.) This is shown in Figures 6A and 6B of that patent:

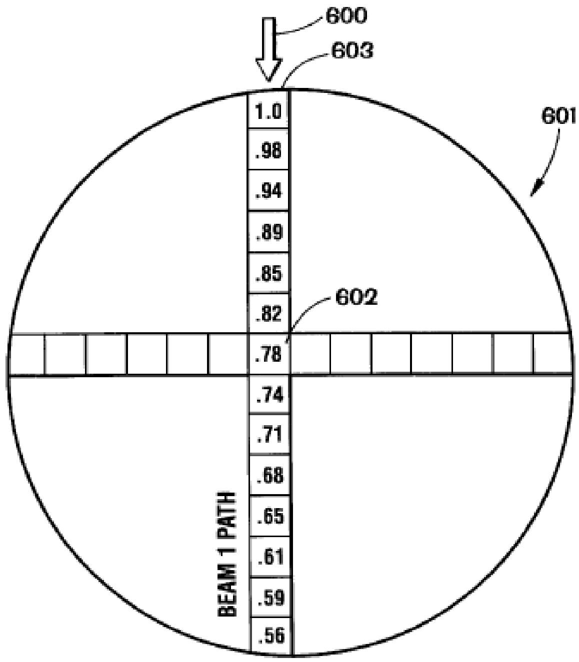


FIG. 6A

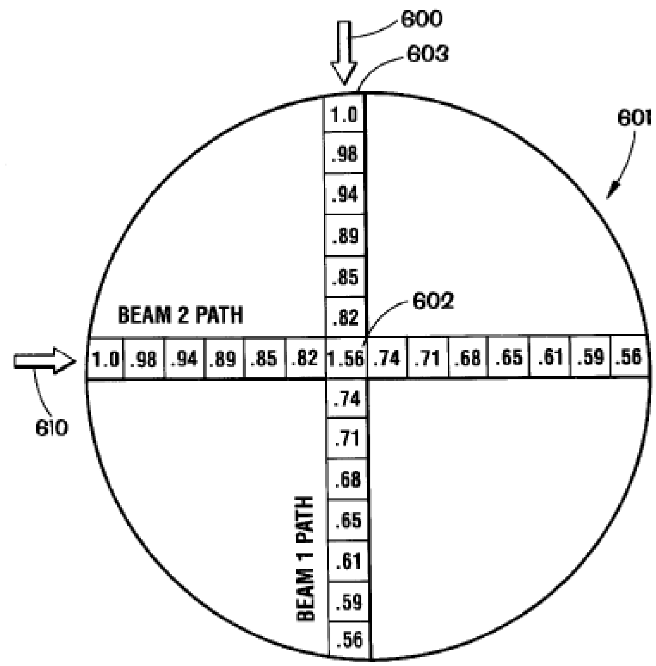


FIG. 6B

(*Id.*, Figs. 6A, 6B.)

It is thus unclear – and the '175 patent does not describe – how one might evaluate a "dosimetric cost term representing dosimetric fitness of the respective intensity map," as claimed, if "**intensity map**" refers to a representation of a single "respective" beam rather than a "**representation of dose distribution**" as proposed.

This construction is further supported by claim 16, which depends from claim 13. Claim 16 includes a reference to "***the*** respective ***dose*** intensity map," which through antecedent basis, makes clear that the individual, "respective intensity map" originally recited in independent claim 13 represents dose – and not beam intensity.

A construction contrary to the one proposed by Petitioner would not only exclude the embodiments of "dose distribution intensity maps" provided in the '175 patent, *e.g., Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276 (Fed. Cir. 2008), but present serious concerns of invalidity under §112. For example, as explained, an interpretation that limits "intensity map" to a representation of a single beam would render the claims nonsensical and therefore indefinite. *Trs. of Columbia Univ.*, 811 F.3d at 1367. Additionally, the patent neither describes nor enables the use of a "dosimetric cost term representing dosimetric fitness," as claimed, of a single-beam representation. *See, e.g., Trs. of Boston Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1362-65 (Fed. Cir. 2018).

Petitioner is mindful that the Board "need only construe the claims to the extent necessary to determine whether to institute *inter partes* review." *Abbott Vascular, Inc. v. FlexStent, LLC*, IPR2019-00882, Paper 11 at 5 (P.T.A.B. Oct. 7, 2019) (citing *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017)). The Board thus need not explicitly adopt Petitioner's construction to evaluate how the prior art has been applied to the claims, *see Oatey*, 514 F.3d at 1276 – ***unless*** the Patent Owner attempts to distinguish the prior art by relying on an interpretation of "intensity map" (either express or implied) that reads out the construction proposed by Petitioner.

VIII. THE CHALLENGED CLAIMS ARE UNPATENTABLE

This Petition presents four Grounds of obviousness. Ground 1 relies on the combination of Webb 2001 and Mohan. Ground 2 builds upon Ground 1 by adding Webb 1993. Grounds 3 and 4 mirror Grounds 1 and 2, respectively, and additionally cite the Siebers reference.

A. Prior Art and Date Qualification for Ground 1

Ground 1 addresses claims 13-15 and as noted, relies on Webb 2001 and Mohan, briefly summarized below.

1. Webb 2001 [Ex 1003]

Webb 2001 is an article entitled "A Simple Method to Control Aspects of Fluence Modulation in IMRT Planning" from the scientific journal *Physics in Medicine & Biology*. Webb 2001 qualifies as prior art under §102(b). (Ex. 1011, Declaration of Sylvia Hall-Ellis ("Hall-Ellis"), ¶¶42-47.)

Webb 2001 recognized that in optimizing an IMRT treatment plan, "[t]here is a tradeoff between obtaining desirable features in beam-space and high conformality in dose-space." (Webb 2001, N187 (Abstract).) Webb 2001 teaches a cost function that places control of that tradeoff in the hands of the user:

> 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…. The method is very transportable provided a treatment-planning system manufacturer provides access to the specification of the cost function.

(Webb 2001, N194.)

Webb 2001 calls its cost function a "hybrid cost function," and it includes a term that controls features of the dose-space as well as a term that controls features of the beam-space. (Webb 2001, *e.g.*, N189.) This is shown below:

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

(*Id.*, N189.)

2. Mohan [Ex 1004]

Mohan is an article entitled "The Impact of Fluctuations on Intensity Patterns on the Number of Monitor Units and the Quality and Accuracy of Intensity Modulated Radiotherapy" from the scientific journal *Medical Physics*. Mohan qualifies as prior art under §102(b). (Hall-Ellis, ¶¶48-53.)

Mohan's Abstract states: "The purpose of this work is to examine the potential impact of the frequency and amplitude of fluctuations ('complexity') in intensity distributions on intensity-modulated radiotherapy (IMRT) dose distributions." (Mohan, 1226 (Abstract).) Mohan is cited for its explanation of the underlying physical principles that demonstrate how the term $\boldsymbol{w_3[w_1 S_+ - w_2 F_{\min}]}$ in the cost function of Webb 2001 operates to enhance the beam-space properties, i.e., delivery efficiency, of a treatment plan.

B. Ground 1: Claims 13-15 Over Webb 2001 and Mohan

1. 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:" (Claim 13 [preamble])

To the extent the preamble of claim 13 is limiting, it is disclosed and rendered obvious by **Webb 2001**. The Abstract of Webb 2001 states:

> Many inverse-planning algorithms and commercial systems generate intensity-modulated beam profiles that have considerable structure. This is the desirable outcome of the quest for high dose-space conformality. However, when these profiles are realized experimentally using the dynamic multileaf collimator (DMLC) method of delivery the monitor-unit efficiency can be quite small, with unwanted consequences. Also the interpretation of these fields leads to the generation of small field segments, again with undesirable consequences. In this note it is shown that *the features of beam-space can be user-controlled to minimize these problems. There is a tradeoff between obtaining desirable features in beam-space and high conformality in dose-space*.

(Webb 2001, N187 (Abstract); *see also id.*, N188.)

As shown, Webb 2001 plainly recognized, and teaches, the existence of "**a**

trade-off between treatment plan delivery efficiency and dosimetric fitness" in optimizing radiation treatment plans. Webb 2001 explains that computed beam profiles with "high dose-space conformality" (i.e., those that achieve "the desirable outcome") result in delivery (1) in which "monitor-unit efficiency can be quite small, with unwanted consequences," and (2) using "small field segments, again with undesirable consequences." (Webb 2001, N187 (Abstract).) A person of ordinary skill would have understood and found it obvious that using small MLC shapes or segments to deliver radiation corresponds to an increased number of segments required to deliver a complete treatment, because each individual segment would deliver a smaller portion of the overall radiation. (Solberg, ¶75.)

Thus, "[t]here is a tradeoff between obtaining desirable features in beam-space and high conformality in dose-space." (Webb 2001, N187 (Abstract).) A person of ordinary skill would have understood that the level of "conformality" in "dose-space," in the parlance of Webb 2001, refers to the "**dosimetric fitness**" of a computed treatment plan. (Solberg, ¶76.) A person of ordinary skill would have also understood that "desirable features in beam-space" refers to characteristics of the computed beams that enhance their "**delivery efficiency**." (Webb 2001, N190 ("[T]he beam-space characteristics dramatically improve… illustrating the improved delivery efficiency and the use of field components of much larger physical dimensions….”); Solberg, ¶77 (citing Webb 2001, N190, N188, N194).)

By identifying the tradeoff between “obtaining desirable features in beam-space and high conformality in dose-space” (Webb 2001, N187 (Abstract)), therefore, Webb 2001 teaches the existence of “**a trade-off between treatment plan delivery efficiency and dosimetric fitness**” in optimizing treatment plans, as claimed.

Webb 2001’s discussion of the tradeoff between delivery efficiency and dosimetric fitness, including its identification of the undesirable consequences of inefficient delivery, is remarkably similar to the description provided in the ’175 patent. (Solberg, ¶78 (citing ’175, 1:13-26).) Indeed, Webb 2001 specifically identified “CORVUS” – a product of NOMOS, the assignee on the face of the ’175 patent (Solberg, ¶78 n.3) – as a system that may compute treatment plans with traits associated with inefficient delivery. (Webb 2001, N188 (“[M]any of the field components (e.g. computed by CORVUS) that comprise a delivery have very small field shapes….”).)

Webb 2001 thus expressly identified the very problem the ’175 patent (originally assigned to NOMOS) purports to solve. (Solberg, ¶79 (citing ’175, 1:29-32).) Webb 2001 also taught the very solution the ’175 patent alleges to be inventive – “**providing control**” of the trade-off between delivery efficiency and dosimetric fitness:

> Altogether it would be desirable for there to be some method to *control* the degree of modulation and the minimum size of the field components. The purpose of this note is to show that this can be achieved fairly simply by ensuring that as much attention is given to the characteristics of the iteratively developed beam profiles as to the characteristics of the developed dose distribution. However, from the outset it must be recognized that one cannot expect that more desirable beam-space properties will be consistent with maintaining the best dose-space conformality. Inevitably we shall find that a tradeoff arises. It will be shown how this can be under the *control of the user*.

(Webb 2001, N188; *see also id.,* N187 (Title) ("A simple method to control aspects of fluence modulation in IMRT planning"); N187 (Abstract) ("In this note it is shown that the features of beam-space can be user-controlled to minimize these problems."); N189; Solberg, ¶80.)

Webb 2001 thus discloses and renders obvious **"[a] method of providing control of a trade-off between treatment plan delivery efficiency and dosimetric fitness to optimize a radiation treatment plan**." (Solberg, ¶¶81, 88.) Any attempt to import a requirement of a graphical user interface (GUI) into the recitation of "**providing control**" provides no non-obvious distinction. (Solberg, ¶¶85-87.)

As relevant to the recitation of "**a continuum between delivery efficiency and dosimetric fitness**," Webb 2001 teaches that control of the tradeoff is provided using a "hybrid cost function" that adds a "beam-space" term to the "dose-space" term, each with parameters that can be defined by the user. (Webb 2001, N189 ("The *new development* is to compute two extra parameters at each iteration which characterize beam-space and then make use of them in a hybrid cost function.") (emphasis in original).) Webb 2001 states:

> 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…. The method is very transportable provided a treatment-planning system manufacturer provides access to the specification of the cost function.

(Webb 2001, N194.)

The user can thus specify any range of values to be the parameters of the cost function taught by Webb 2001, which as mentioned, includes a term used to characterize features of the "dose space." (Webb 2001, N194, N189.) This in turn allows the user to choose the desired "degree" of conformality as balanced against the desired "degree" of delivery efficiency. (Solberg, ¶83.) Webb 2001 thus discloses and renders obvious providing control of the tradeoff "**to optimize a**

radiation treatment plan within a continuum between delivery efficiency and dosimetric fitness."[5] Additional details about Webb 2001's technique, including its "hybrid cost function," are discussed in connection with the limitations below.

(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; and" (Claim 13[a])

Claim 13[a] is disclosed and rendered obvious by **Webb 2001** in view of **Mohan**. Webb 2001 teaches "**assigning a delivery cost term within an optimizer to each of a plurality of intensity maps representing a potential radiation beam arrangement**," and Mohan is cited for its explanation of the underlying physical principles that demonstrate how the "**delivery cost term**" in Webb 2001 in fact operates "**based on the complexity**" of each "intensity map."

"an optimizer": As explained, an "**optimizer**" means an "**iterative optimization algorithm**." This limitation is disclosed in Webb 2001:

> Inverse planning has been carried out iteratively using the technique described by Webb *et al* (1998). This is an iterative method which

[5] The use a hybrid cost function in Webb 2001 that contains a user-defined term for "beam-space" mirrors one of the methods described in the '175 patent for providing control of tradeoff "**within a continuum**." (Solberg, ¶83 n.4.)

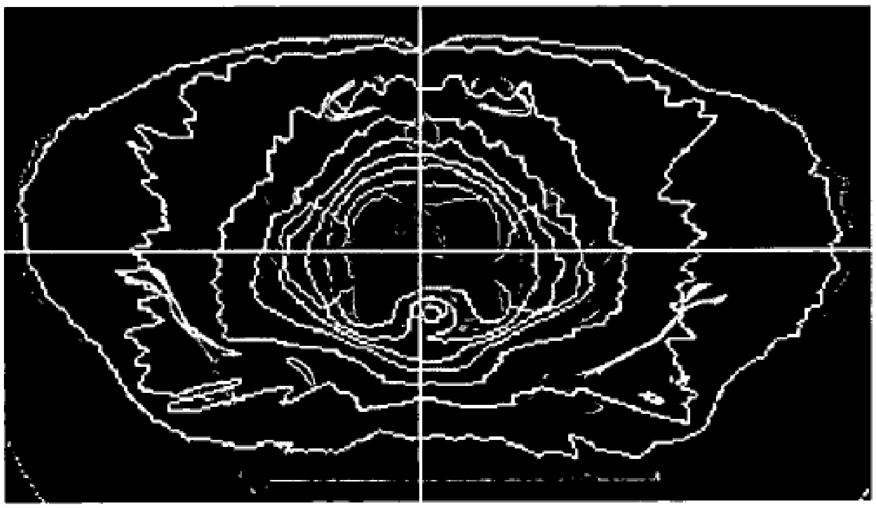
> predetermines the number of coplanar gantry angles and creates the modulated 1D profiles which, when combined, lead to a conformal 2D dose distribution. At each iterative cycle, grains of beamweight are offered to one of the fields, randomly selected from the set, and to one randomly chosen beam element (bixel). The cost of the change in dose-space is computed and, if lower than the previous estimate, the grain is accepted. After a predetermined number of iterations (48000), chosen so each bixel site is visited many times (at least 250), 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. All this is fairly standard….

(Webb 2001, N188.)

Webb 2001 thus describes an "**iterative optimization algorithm**" that outputs a set of beam profiles corresponding to the optimized treatment plan. As Webb 2001 makes clear, "[a]ll this is fairly standard." (*Id.*) This is confirmed by U.S. Patent 6,038,283 (incorporated into the '175 patent by reference), which freely admits that an "**iterative optimization algorithm**" for treatment planning (known as "SARP") was well-known in the art as early as 1997. (Ex. 1012, U.S. 6,038,283, 8:61-67, 12:27-45.)

"each of a plurality of intensity maps representing a potential radiation beam arrangement": As explained above, the term "**intensity map**" in the context of the

’175 patent means a “**representation of dose distribution**.” To facilitate clarity in Petitioner’s mapping of the prior art to this claim limitation, reproduced below is one example of a “dose distribution intensity map” given by the ’175 patent:



(’175, Fig. 4C; *see also id.*, 2:3-4.) As explained below, Webb 2001 discloses precisely such an “**intensity map**,” i.e., “**representation of dose distribution**,” and evaluates multiple such “intensity maps,” one at each iteration, as it progresses through the optimization algorithm.

Webb 2001 describes a “fairly standard” optimization process as follows:

> 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. At each iterative cycle, grains of beamweight are offered to one of the fields, randomly selected from the set, and to one randomly chosen beam element (bixel). The cost of the change in dose-space is computed and, if lower

> than the previous estimate, the grain is accepted. After a predetermined number of iterations… the outcome is a set of beam profiles and the corresponding dose distributions together with statistics characterizing the distribution….

(Webb 2001, N188.)

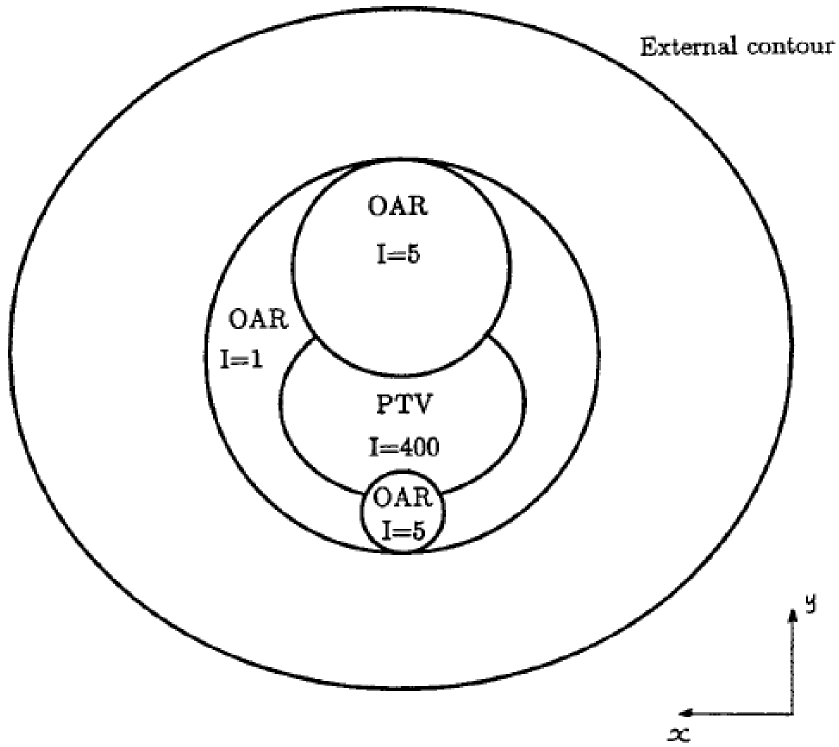
Based on the above passage, a person of ordinary skill would have understood that the following steps are performed during each iteration:

- A new set of fields (or "beam profiles") is generated by making a change to the set of fields from the previous iteration.
- A new dose distribution is computed based on the new set of fields (or "beam profiles").
- The cost of the new dose distribution is computed using a cost function.
- The cost of the new dose distribution is compared to the cost of the dose distribution from the previous iteration. And if the cost for the current iteration is lower, the set of fields (or "beam profiles") generated during the current iteration (based on a change made to the previous iteration) is accepted, and passed to the next iteration for additional modification, until an optimized set of fields is generated.

(Solberg, ¶94.)

Within this "fairly standard" optimization process, a claimed "**intensity map**," i.e., "**representation of dose distribution**," is computed during each iteration based on the set of beam profiles generated at that iteration. (Webb 2001, N188 ("This is an iterative method which… creates the modulated 1D profiles which, when combined, lead to a conformal 2D dose distribution…. After a predetermined number of iterations… the outcome is a set of beam profiles and the corresponding dose distributions….").) As described in Webb 2001, the dose distribution at each iteration is represented computationally as a grid of "dose elements" – akin to the pixels of an image – in which each dose element has a value representing the amount of dose that would be received at that location from the current multi-beam arrangement. (Webb 2001, N189 ("[D]ose distributions were computed on a 300×300 grid with a pixel size of 1 mm."), ("…*(i, j)*th dose element….").)

A simplified model dose distribution is shown pictorially in Figure 1:



(Webb 2001, N189 (Fig. 1).) A person of ordinary skill would have understood that each line drawn above is an "isodose" line, which connects individual dose elements (not shown) having the same dose value (e.g., "1" or "5"). (Solberg, ¶96.)

Because the dose distribution shown above is based on a simplified model geometry, the isodose lines are shown as being smooth. But a person of ordinary skill would have understood and found it obvious that the dose distributions computed during real-world optimization will not always have smooth isodose lines, like the example shown in Figure 4C of the '175 patent, reproduced towards the beginning of this section. (Solberg, ¶97.)

Next, each representation of dose distribution in Webb 2001 (i.e., grid "*D(i,* *j)*") "**represent[s] a potential radiation beam arrangement**" because as explained above, it captures the dose that would result from the particular set of beam profiles being evaluated at each iteration. (Webb 2001, N188 ("[T]he modulated 1D profiles which, when combined, lead to a conformal 2D dose distribution."), *id.* ("At each iterative cycle, grains of beamweight are offered to one of the fields…."), N189 ("*D(i, j)* is the dose from the grains so far placed…"), N188 (cost function (1)), N188 (cost function (2)).) And because the optimization algorithm cycles through multiple iterations, it would compute and evaluate multiple, i.e., "**a plurality** of intensity maps." (Solberg, ¶98.)

Petitioner has thus explained how the details of the "fairly standard" optimization algorithm described in Webb 2001 map onto to the limitation of "**each of a plurality of intensity maps representing a potential radiation beam arrangement**." These details are also admitted to be prior art by the '175 patent. (Solberg, ¶99 (citing Ex. 1012, U.S. 6,038,283, 9:61-65).) As such, the techniques mapped above to the claim language were not only expressly disclosed in Webb 2001, but also firmly within the knowledge of persons of ordinary skill.

<u>"assigning a delivery cost term" within the iterative optimization algorithm to each "intensity map":</u> The step of "**assigning a delivery cost term**" occurs within the optimization algorithm when the cost of a new dose distribution is computed

during each iteration using the "hybrid cost function." (Webb 2001, N188 ("At each iterative cycle, grains of beamweight are offered…. The cost of the change in dose-space is computed….”), N189 ("[F]or this work, a hybrid cost function χ was computed which combines features from dose-space and these two features from beam-space."); Solberg, ¶100.) This "hybrid cost function" is:

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

"intensity map" "delivery cost term"

(Webb 2001, N189.)

The claimed "**delivery cost term**" corresponds to the portion of the overall function annotated in blue: $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$. (Solberg, ¶101.) Webb 2001 refers to this term as the "beam-space cost function." (Webb 2001, N190.) And it controls the characteristics of the beam profiles generated during optimization to improve their delivery efficiency:

> So, for example, if w_3 is set to zero the iterations ignore beam-space constraints and proceed to minimize only the cost in dose-space…. 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 [intensity-modulated beams] become smoother and the maximum value of the minimum fieldsize increases as desired….

> ...Columns 3–5 show the effect of increasing the weight to the contribution from beam-space to the cost function χ. <u>As w_3 rises</u> through 10, 20 to 30, the cost in dose-space rises… but, as demanded, <u>the beam-space characteristics dramatically improve</u>. S_+ falls to 218 and F_{min} climbs to 46, <u>illustrating the improved delivery efficiency</u> and the use of field components of much larger physical dimensions….

(Webb 2001, N190.)

The "**intensity map[]** [i.e., "representation of dose distribution"] **representing a potential radiation beam arrangement**" is also incorporated into the overall cost function, and corresponds to the portion annotated in orange: ***D*(*i*, *j*)**. (Solberg, ¶102.) A person of ordinary skill would have understood and found it obvious that when the value of hybrid cost function is computed during each iteration, the "**delivery cost term**" ($w_3[w_1S_+ - w_2F_{min}]$) is "**assign[ed]**" to the "intensity map" (represented by $D(i, j)$) so that the computed value of the delivery cost term can be included as part of the overall cost for that "intensity map." (Webb 2001, N189 ("The *new development* is to <u>compute two extra parameters at each iteration which characterize beam-space and then make use of them in a hybrid cost function</u>.") (italics in original); Solberg, ¶102.)

<u>the assignment of the delivery cost term "based on complexity of each respective intensity map"</u>: As explained, the term "**intensity map**" in the context of the '175 patent means a "**representation of dose distribution**," and corresponds to

the term ***D*(*i*, *j*)** in Webb 2001's hybrid cost function:

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

"intensity map" "delivery cost term"

(Webb 2001, N189.)

As relevant to assigning the delivery cost term "**based on complexity of each respective intensity map**," as claimed, the '175 patent provides the following written description: "A delivery cost term is assigned to an intensity map based upon the complexity of the intensity map. Maps with more intensity changes generally require more segments to deliver, and thus are assigned a larger delivery cost term." ('175, 2:51-55.) Based on the written description, therefore, a person of ordinary skill would have understood that an "intensity map," i.e., "representation of dose distribution," is considered more "**complex**" when the corresponding set of beam profiles that would be used for delivery contains more **changes in intensity**. (Solberg, ¶104; *see also* '175, 6:42-48 (dependent claim 18, reciting "more complex beam arrangements").) As explained below, this is precisely how the delivery cost term in Webb 2001 operates.

As shown in blue annotation above, the "**delivery cost term**" corresponds to $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$. w_1, w_2, and w_3 are user-defined weights. (Webb 2001, N190.)

Their values are thus fixed throughout the optimization process, and do not change at any particular iteration based on the characteristics of the dose distribution (represented by $D(i, j)$). (Solberg, ¶105.)

But the values of $\boldsymbol{S_+}$ and $\boldsymbol{F_{\mathbf{min}}}$ do depend on the particular dose distribution ("**intensity map**"), $\boldsymbol{D(i, j)}$, computed at each iteration. Specifically, their respective values vary based on the intensity profiles of each of the beams that would be used to collectively deliver the dose distribution. Each of $\boldsymbol{S_+}$ and $\boldsymbol{F_{\mathbf{min}}}$, and thus their weighted combination as used in the cost function, operate to drive the dose distributions computed at each iteration towards those capable of being delivered with fewer changes in intensity, i.e., less "**complex**" dose distributions, as explained further below.

Assignment of $\boldsymbol{S_+}$ based on Complexity: The value of $\boldsymbol{S_+}$ at each iteration is given by:

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

(Webb 2001, N189.) $\boldsymbol{N_B}$ is the total number of beams in the multi-beam arrangement, and **20** (in the example used by Webb to illustrate his technique) is the number of beam elements, or "bixels," in each beam. (*Id.* ("N_B is the number of IMBs [intensity-modulated beams], each with 20 elements….").)

"**(Δ_+*I*)*m,n*** is the change in fluence at the *m*th bixel [i.e., beam element] of the *n*th beam *if positive*. Negative and zero changes are not included in the sum." (Webb 2001, N189 (italics in original).) Accordingly, the value of $\boldsymbol{S_+}$ is calculated by traversing through every bixel of every beam of the multi-beam arrangement corresponding to the dose distribution $\boldsymbol{D(i, j)}$ at a particular iteration, bixel by bixel and beam by beam, and summing the positive changes in intensity between neighboring bixels within each beam. (Webb 2001, N194 ("The computation of S_+ and $F_{\min}$ are relatively trivial. <u>The former simply requires us to sum positive fluence changes for all beams</u>…."); Solberg, ¶108.)

As to the rationale behind $\boldsymbol{S_+}$, Webb 2001 explains: "It is well known . . . that <u>the treatment time is directly given by the sum of the positive-going fluence changes</u> added to the fixed time for a leafpair to sweep the field at maximum speed." (Webb 2001, N189.) By minimizing the component of treatment time that is not fixed, i.e., "the sum of the positive-going fluence changes," $\boldsymbol{S_+}$ as used in the cost function drives the optimization algorithm towards dose distributions that require less time to deliver. (Solberg, ¶109.)

<u>**Mohan**</u> further explains the physical principles behind the operation of $\boldsymbol{S_+}$, and shows how it provides a good metric of changes in intensity, and thus "**complexity**" as claimed. (*See* '175, 2:51-55.) Mohan elaborates on what Webb

2001 states is "well known" (Webb 2001, N189) – that the theoretical minimum beam-on time (as quantified in MUs) required to deliver a "modulated 1D [beam] profile[]" (Webb 2001, N188) is given by:

$$M^l = (1-\tau)\frac{x_{i_{\text{last}}} - x_{i_{\text{start}}}}{v_{\max}} + \sum_{\substack{i=i_{\text{start}} \\ \Omega(x_{i+1})>\Omega(x_i)}}^{i_{\text{last}}-1} [\Omega_e(x_{i+1}) - \Omega_e(x_i)]. \qquad (7)$$

(Mohan, 1229 (left column).) Where:

- $X_{i_{\text{start}}}$ refers to the starting position of the leaf pair, which is the point just before the first nonzero beam element.
- $X_{i_{\text{last}}}$ refers to the terminal position of the leaf pair, which is the point just after the last nonzero beam element.
- Ω_e refers to the intensity to be delivered at each point in the path of leaf travel.

(Mohan, 1227-1229.)[6]

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[6] A person of ordinary skill would have understood and found it obvious that each "modulate 1D profile" generated in Webb 2001 (Webb 2001, N188) would be delivered by a single leaf pair. (Solberg, ¶110 n.8.) Towards the end of his paper,

One can thus see that the first term (shown in green) in the equation laid out in Mohan is what Webb 2001 describes as "the fixed time for a leafpair to sweep the field at maximum speed" (Webb 2001, N189; Solberg ¶111.) And the second term (shown in purple) is the very same "$(\Delta_+ \boldsymbol{I})\boldsymbol{m,n}$" term used in Webb 2001's formulation of $\boldsymbol{S}_+$. The only difference is that $\boldsymbol{S}_+$ adds up not just the "positive-going fluence changes" in a *single* beam, but does so for *all* beams. (Webb 2001, N189.)

Mohan explains that "the contribution of the second term [i.e., $\boldsymbol{S}_+$ in Webb 2001] <u>depends upon the complexity of the opening density profile</u>." (Mohan, 1229 (left column).) "[I[f the opening density falls and then rises for some of the points, the beam-on time" – and likewise $\boldsymbol{S}_+$ – "will <u>increase depending upon both the frequency and the amplitude of the fluctuations</u>." (*Id*.)

The correlation between beam-on time (and likewise $\boldsymbol{S}_+$) and the amount of change in intensity is depicted graphically in Figure 2 of Mohan:

Webb explains how his technique demonstrated using one-dimensional beams can be generalized to "two-dimensional fluence modulations," i.e., two-dimensional beams, and this is discussed further for Grounds 3 and 4 below. (Webb 2001, N194.)

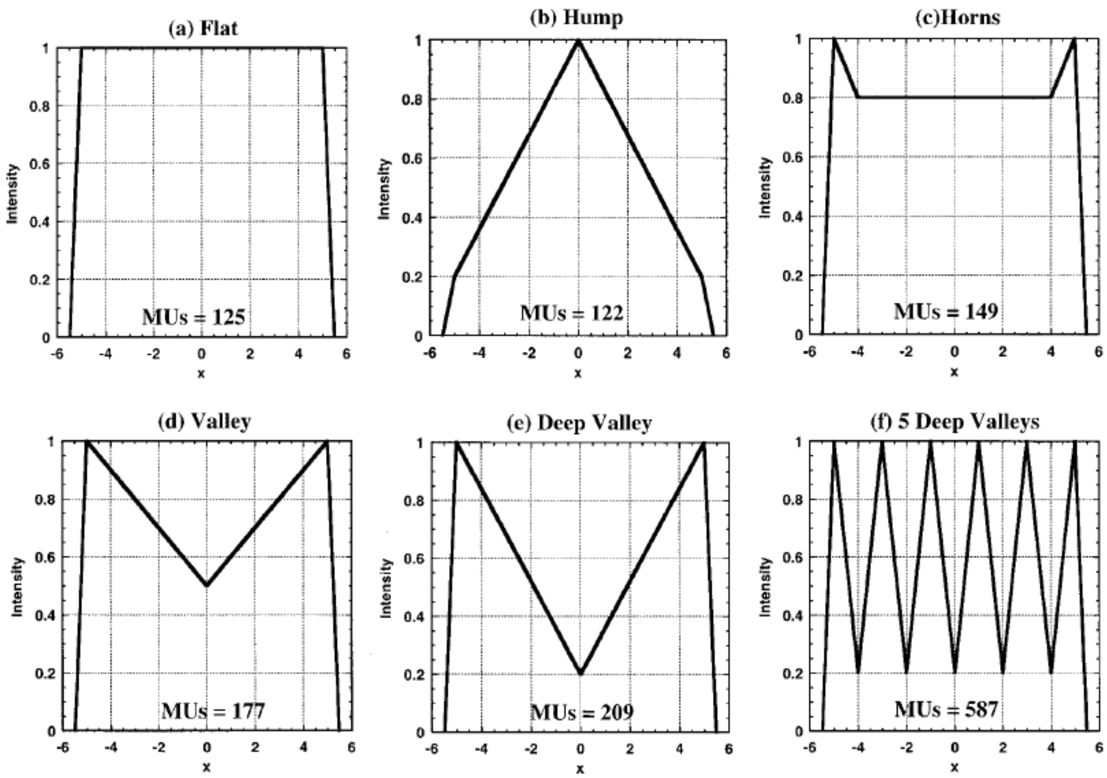


FIG. 2. Beam-on time (MU settings) needed to effectively deliver 100 MUs peak value (corresponding to an intensity of 1) for the intensity patterns shown. Calculations were done using the sliding window technique, a maximum leaf speed of 2 cm/s and a dose rate of 240 MU/min. Corrections for leaf transmission and rounded leaf tip were included.

(Mohan, 1231 (Fig. 2).) Mohan states: "As may be intuitively obvious, and is clear from figures (b)-(f), the number of MUs required to deliver the same maximum intensity increases as the amplitude (depth of valleys) and the frequency (number of valleys) of fluctuations increases." (Mohan, 1231 (left column).)

Thus, as shown, more intensity changes result in higher values for beam-on time as quantified in MUs. (Solberg, ¶114.) And because beam-on time is simply "the sum of the positive-going fluence changes [i.e., $\sum(\Delta_{+}\boldsymbol{I})\boldsymbol{m}$] added to the fixed time for a leafpair to sweep the field" (Webb 2001, N189; *see also* Mohan, 1229 (equation 7)), more intensity changes would similarly result in larger values for $\boldsymbol{S}_{+}$

as given by:

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

(Webb 2001, N189.)

Accordingly, the value of $\boldsymbol{S_+}$ at each iteration would depend on the nature of the intensity changes associated with a particular dose distribution, and thus get assigned "**based on complexity of each [] intensity map**" as claimed. (*See* '175, 2:51-55.)

And the use of $\boldsymbol{S_+}$ in a cost function to enhance delivery efficiency makes sense. As previously mentioned, and then shown with reference to the theoretical underpinning provided in Mohan, $\boldsymbol{S_+}$ minimizes the component of treatment or "beam-on" time that is not fixed (Webb 2001, N189; Mohan, 1229), and thus drives the optimization algorithm towards dose distributions that require less time to deliver. (Solberg, ¶116.) This mirrors techniques purportedly described in the '175 patent for providing user control of delivery efficiency. (Solberg, ¶116 (citing '175, 1:42-44, 2:28-36).)

Moreover, claim 14, which depends from claim 13, recites that "**<u>the delivery cost term is a function of delivery time required to deliver radiation</u> according to a beam arrangement represented by the respective intensity map**." As shown above, $\boldsymbol{S_+}$ operates to reduce delivery time, and this further confirms that $\boldsymbol{S_+}$ is properly mapped to the limitation of "**assigning a delivery cost term… based on complexity of each respective intensity map**" originally recited in claim 13. (*See also* '175, 2:51-55.)

Assignment of $\boldsymbol{F_{min}}$ based on Complexity: The value of $\boldsymbol{F_{min}}$ likewise depends on the changes in beam intensity associated with the dose distribution at a particular iteration. $\boldsymbol{F_{min}}$ is given by:

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

(Webb 2001, N189.) $\boldsymbol{d_{min}}$ is the "minimum fieldsize" for the hypothetical delivery of one beam, i.e., the size of the smallest MLC segment in a sequence of segments that could be used to deliver the beam. (*Id.*) The calculation of $\boldsymbol{F_{min}}$ thus identifies, for each beam in the multi-beam arrangement, the delivery method that would yield the largest minimum fieldsize, **max($\boldsymbol{d_{min}}$)**, and sums those values across all beams, $\boldsymbol{N_B}$, of the multi-beam arrangement. (*Id.* ("[A] method of delivery which maximizes this minimum fieldsize d_{min} (the leaf-sweep method) was selected. Then the second quantity computed was the sum over all beams of these values."), N194 ("The computation of S_+ and F_{min} are relatively trivial…. [T]he latter is given by pairing the rising and falling IMB edges in the usual leaf-sweep mode, finding the minimum fieldsize and summing these for all beams.”).)

Accordingly, a person of ordinary skill would have understood that the value of $\boldsymbol{F}_{\mathbf{min}}$ would generally increase as the size of the segments that would be used for beam delivery increases. (Webb 2001, *e.g.*, N190 (“The relative weights of w_1 and w_2 control whether beam smoothing or maximization of minimum fieldsize is the priority.”), N194 (“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.”); Solberg ¶119.) And as the size of component segments increase, the corresponding dose distributions would require fewer segments to deliver, because each segment would deliver a greater quantum of radiation. (Solberg ¶119.) $\boldsymbol{F}_{\mathbf{min}}$ (more precisely, $-\boldsymbol{F}_{\mathbf{min}}$) thus drives the optimization algorithm towards dose distributions that require fewer segments to deliver.

The operation of these principles is expressly confirmed in **Mohan**, which demonstrates how $\boldsymbol{F}_{\mathbf{min}}$, like $\boldsymbol{S}_{+}$ discussed previously, provides another good metric of intensity changes and thus “**complexity**” as claimed. (*See* ’175, 2:51-55.)

Mohan refers to MLC segments as “windows.” (Mohan, *e.g.*, 1226 (Abstract); Solberg ¶121.) Mohan explains that “for complex intensity patterns, the average window width tends to be smaller….” (Mohan, 1226 (Abstract); *see also* *id.,* 1226 (right column) – 1227 (left column).) The correlation between window or segment size and the amount of change in intensity is depicted graphically in Figure 3 of Mohan:

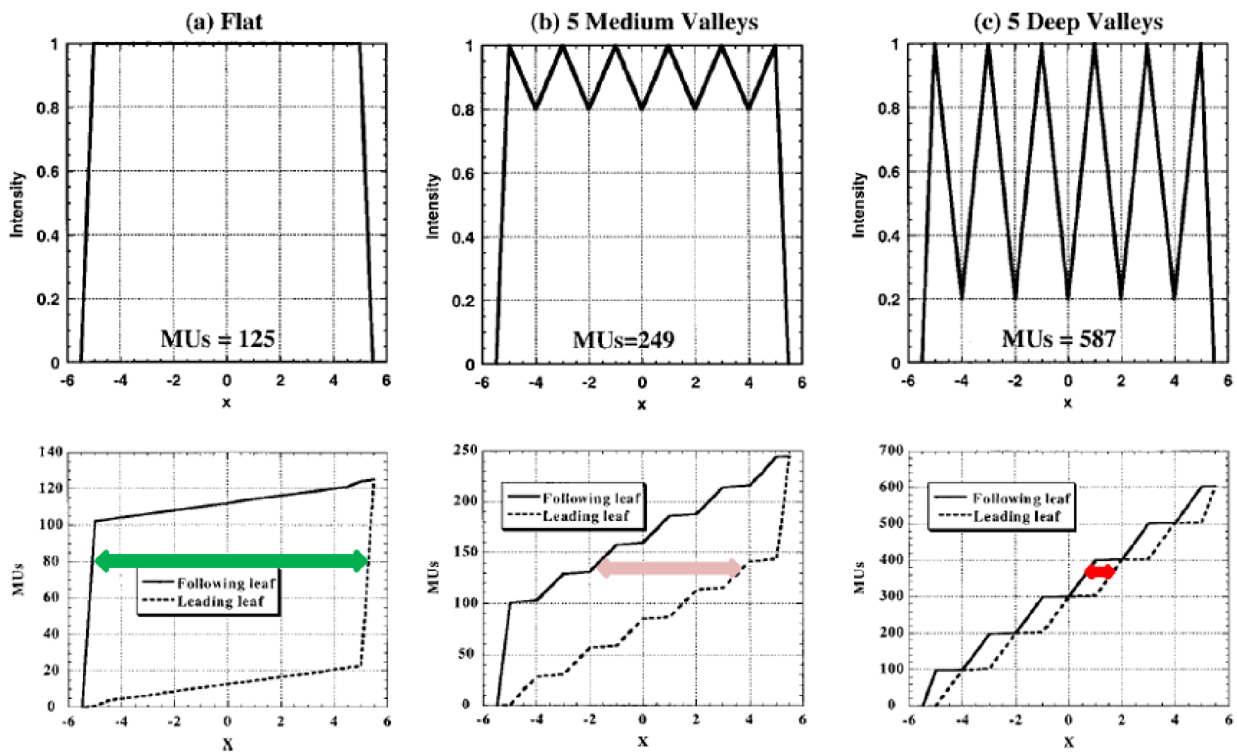


FIG. 3. Dependence of leaf trajectory and window width on the fluctuations of the intensity pattern.

(Mohan, 1232 (Fig. 3).)

Thus, as shown, more intensity changes result in smaller window or segment sizes. (Solberg ¶¶120-121.) And because $\boldsymbol{F}_{\mathbf{min}}$ sums the maximum size of the smallest segment from each beam across all beams, more intensity changes would similarly result in smaller values for $\boldsymbol{F}_{\mathbf{min}}$ as given by:

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

(Webb 2001, N189.)

Accordingly, the value of $\boldsymbol{F_{min}}$ at each iteration would depend on the nature of the intensity changes associated with a particular dose distribution, and thus get assigned "**based on complexity of each [] intensity map**" as claimed. (*See* '175, 2:51-55; Solberg ¶123.) Note that unlike $\boldsymbol{S_+}$, the value of $\boldsymbol{F_{min}}$ is *subtracted* in the delivery cost term. (Webb 2001, N189.)

And the use of $\boldsymbol{F_{min}}$ in a cost function in this manner to enhance delivery efficiency makes sense. As previously mentioned, and then showed with reference to the principles explained in Mohan, $\boldsymbol{F_{min}}$ (more precisely, lower values for $\boldsymbol{-F_{min}}$) maximizes the size of the segments that would be used to deliver the computed beam profiles (*e.g.*, Webb 2001, N189-N190; Mohan, 1232), and thus drives the optimization algorithm towards dose distributions that require fewer segments to deliver. (Solberg ¶124.) This also mirrors techniques purportedly described in the '175 patent for providing user control of delivery efficiency. (Solberg ¶124 (citing '175, 2:49-51).)

Moreover, claim 17 which depends from claim 13, recites that "**the delivery cost term <u>represents a segment count</u>**." As shown above, $\boldsymbol{F_{min}}$ operates to reduce segment count, and this further confirms that F_{min} is properly mapped to the limitation of "**assigning a delivery cost term… based on complexity of each respective intensity map**" originally recited in claim 13. (*See also* '175, 2:51-55.)

Accordingly, as explained at length, the values of S_+ and F_{min} both depend on the "**complexity of each respective intensity map**." The weighted summation of S_+ and $-F_{min}$ into a single value $w_3[w_1S_+ - w_2F_{min}]$, therefore, would also depend on the "**complexity of each respective intensity map**" as claimed. (Solberg ¶126.) In other words, because the individual values of S_+ and $-F_{min}$ would change with the level of claimed "**complexity**," the resultant value of $w_3[w_1S_+ - w_2F_{min}]$ – which depends on the individual values of S_+ and F_{min} – would also change with "**complexity**" as claimed. Because the values for user-defined weights w_1, w_2, and w_3 remain fixed throughout the optimization process, the value of $w_3[w_1S_+ - w_2F_{min}]$ at any particular iteration depends only on the respective values of S_+ and F_{min}.

Moreover, because either of the weights w_1 and w_2 could be set to zero, $w_3[S_+]$ or $w_3[F_{min}]$ (more precisely, $-w_3[F_{min}]$) alone would also independently satisfy the claimed "**delivery cost term**" that gets assigned "**based on complexity of each respective intensity map**." (Webb 2001, N190; Solberg, ¶127.)

<u>Rationale and Motivation to Combine:</u> It would have been obvious to combine Webb 2001 with Mohan. (Solberg, ¶¶128-132.) The combination would have predictably resulted in a method of providing control of a tradeoff between dosimetric fitness and delivery efficiency to optimize a treatment plan within a continuum between dosimetric fitness and delivery efficiency, as taught by Webb 2001. And during the optimization process, the assigned value of the delivery cost term in the hybrid cost function of Webb 2001 would depend on the complexity associated with the dose distribution computed at each iteration of the optimization process, as confirmed by the principles detailed in Mohan.

Webb 2001 and Mohan are analogous references in the field of intensity modulated radiation therapy (IMRT). (Solberg, ¶128.) A person of ordinary skill, looking to implement the optimization technique described in Webb 2001, would have naturally consulted Mohan for guidance in doing so. (*Id.*)

Indeed, Webb 2001 with Mohan both cite other works in IMRT by many of the same authors, including Bortfeld, Convery, and Stein. (Webb 2001 N194-N195; Mohan, 1237 (right column).) The close collaboration exhibited in the field of IMRT, and the closely analogous nature of the two references, would themselves have provided suggestions to combine. (Solberg, ¶129.)

As explained, Petitioner cites Mohan for its robust explanation of the underlying principles that confirm how Webb's cost function would operate to enhance the beam intensities used to deliver computed dose distributions. Mohan provides express motivations to consult its teachings in this regard. The first sentence of the Mohan's Abstract states: "The purpose of this work is to examine the potential impact of the frequency and amplitude of fluctuations ('complexity') in intensity distributions on intensity-modulated radiotherapy (IMRT) dose distributions." (Mohan, 1226 (Abstract); *see also id.*, 1226 (left column).) The very stated "purpose" of Mohan would therefore have motivated a person of ordinary skill to consult its teachings to seek a better understanding of the physical principles underlying the hybrid cost function of Webb 2001. (Solberg, ¶130.) And a person of ordinary skill would have had every expectation that the principles described in Mohan would apply in the context of Webb 2001. (*Id.*)

Mohan further emphasizes that "it is important to understand the causes of the complexity of intensity patterns, their effect on dynamic MLC (DMLC) window width, the number of MUs to deliver a treatment… and their potential impact on quality and accuracy." (Mohan, 1227 (left column).) A person of ordinary skill would have readily appreciated that a developed understanding of these principles would be particularly beneficial – even imperative – to fully realize the benefits enabled by Webb's cost function. (Solberg, ¶131.) This is because that cost function places the tradeoff between dose-space conformality and delivery efficiency fully within the control of the user by allowing the user to specify the relative weights used:

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

(Webb 2001, N189, N194.) When armed with better understanding and deeper knowledge enabled by Mohan's teachings, the person of ordinary skill is in a better position to select appropriate values to achieve the specific results desired. (Solberg, ¶132.)

"Complexity of each respective intensity map": As explained, a person of ordinary skill, based on the written description of the '175 patent, would have understood that an "intensity map," i.e., "representation of dose distribution," is considered more "**complex**" when the corresponding set of beam profiles that would be used for delivery contains more changes in intensity. ('175, 2:51-55, 6:42-48 (dependent claim 18, reciting "more complex beam arrangements").) And this Petition showed how the "**delivery cost term**" in Webb 2001 varies based on the intensity profiles of each of the beams that would be used to collectively deliver the dose distribution.

The Patent Owner may attempt to argue that "**complexity of each respective intensity map**" must be interpreted to refer to the complexity of dose values within the dose distribution itself. But this would provide no basis to distinguish the claim from the prior art. **Mohan** expressly confirms that the complexity of the beam profiles is directly correlated with the complexity of the delivered dose. (Solberg, ¶134.) This is shown in Figure 1:

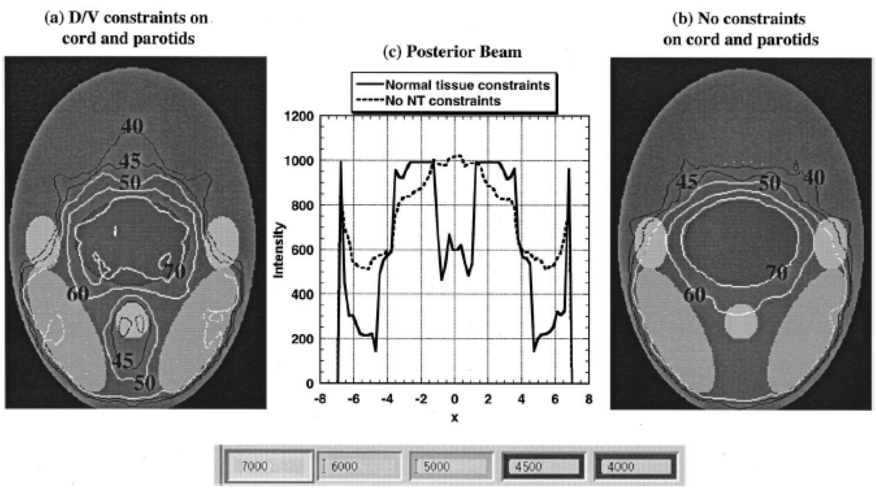
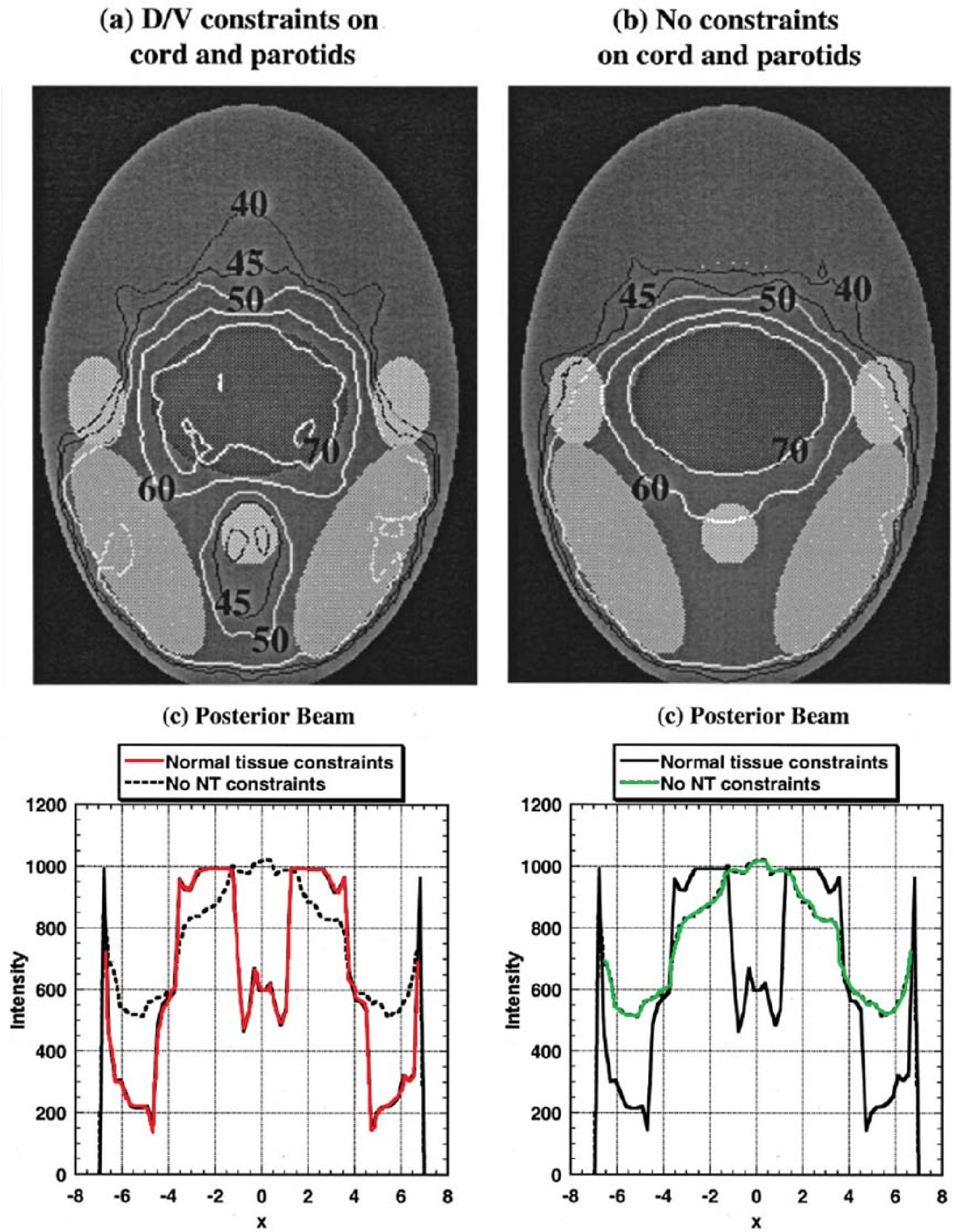


FIG. 1. Two 9-beam, 6 MV IMRT plans illustrating the effect of complexity of anatomy and severity of constraints on the complexity of intensity distributions.

(Mohan, 1230 (Fig. 1).)

Figure 1 shows two resultant dose distributions. Dose distribution **(a)** (shown above at left) was created based on a treatment plan that was subject to dose constraints. (Mohan, 1230 (right column).) Dose distribution **(b)** (shown above at right), on the other hand, was created based on a treatment plan that had the constraints removed. (*Id.*) Figure **(c)** (shown above in the middle) shows the intensity profile for one of the beams (posterior beam) that contributed to the dose distributions shown. The solid line in Figure (c) shows the intensity profile that contributed to dose distribution (a) ("Normal tissue constraints"), and the dotted line shows the intensity profile that contributed to dose distribution (b) ("No NT constraints"). (Solberg, ¶135.)

Dr. Solberg has traced each graph of the beam intensity profile using a different color, and placed them underneath the corresponding dose distribution for ease of comparison:


(a) D/V constraints on cord and parotids
(b) No constraints on cord and parotids
40
45
50
60
70
45
50
45
50
40
60
70
(c) Posterior Beam
Normal tissue constraints
No NT constraints
Intensity
x
1200
1000
800
600
400
200
0
-8
-6
-4
-2
0
2
4
6
8
(c) Posterior Beam
Normal tissue constraints
No NT constraints
Intensity
x

(Solberg, ¶136.) As shown, the smoother beam profile shown at bottom right corresponds to a dose distribution with smoother isodose lines, i.e., less "**complexity**" in the dose values of the dose distribution. Similarly, the more jagged beam profile shown at bottom left corresponds to a dose distribution with more jagged isodose lines, i.e., more "**complexity**" in the dose values of the dose distribution.

Mohan describes the correlation between the complexity of beam profiles to the complexity of the delivered dose:

> *For the case with constraints*, there is a valley in the middle to limit the cord dose. In addition, there are two deep valleys just inside the boundaries of the beam mainly to reduce the dose to the parotids while delivering some dose to the nodes…. *For the case without constraints*, the central valley disappears, and the two valleys on either side of the center are much shallower…. Similar reductions in the complexity of intensity patterns of other beams were found.

(Mohan, 1230 (right column).)

The reduction in "**complexity**" of dose values within the dose distribution as reflected by smoother isodose lines is consistent with the "dose distribution intensity maps" shown respectively in (1) Figures 2A-2C, (2) Figures 4A-4C, and (3) Figures 7-8 of the '175 patent. (Solberg, ¶138.) Within each of the three sets of "dose distribution intensity maps" shown, the isodose lines become smoother as "[e]fficiency becomes more important from top to bottom." ('175, Figs. 2A-2C; *id.*, Figs. 4A-4C.)

Because the complexity of the beam profiles would be directly correlated with the complexity of the delivered dose, therefore, the values of $\boldsymbol{S_+}$, $\boldsymbol{F_{\min}}$, and $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$ would also be "**assigned based on complexity**" in the underlying dose values themselves, to the extent this is required by the claim.

(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, the dosimetric cost term representing dosimetric fitness of the respective intensity map and the delivery cost term representing delivery efficiency." (Claim 13[b])

Claim 13[b] has largely been covered in the analysis of claim 13[a] above. The claimed "**objective cost function**" corresponds to the hybrid cost function in Webb 2001:

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

(Webb 2001, N189.)

This cost function is "**evaluat[ed]**" to calculate the overall cost for the "**intensity map**," i.e., "**representation of dose distribution**" $\boldsymbol{D(i, j)}$ computed at each iteration of optimization. (Webb 2001, N188, N189; Solberg, ¶141.)

The "**dosimetric cost term**" is the term on the left, shown above in brown. This term "**represent[s] [the] dosimetric fitness**" the evaluated dose distribution ***D*(*i*, *j*)** because it quantifies how closely dose distribution ***D*(*i*, *j*)** approximates the prescribed dose distribution $\boldsymbol{D^P(i, j)}$ (as weighted by importance factors $\boldsymbol{I_w(i, j)}$). (Webb 2001, N188-189; Solberg, ¶142.)

The "**delivery cost term**" is the term on the right, shown above in blue. This term "**represent[s] delivery efficiency**" for the reasons discussed for claim 1[b] above. (Solberg, ¶¶143, 101, 105-127.) In short, it controls the characteristics of the beam profiles generated during optimization to improve their delivery efficiency. (Webb 2001, N190.)

2. Claim 14: "A method as defined in claim 13, wherein the delivery cost term is a function of delivery time required to deliver radiation according to a beam arrangement represented by the respective intensity map."

As explained for claim 13[a], the "**delivery cost term**" corresponds to the portion of Webb 2001's cost function shown in blue:

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

"intensity map" "delivery cost term"

(Webb 2001, N189.) And the "**respective intensity map**," i.e., "**representation of**

dose distribution" at each iteration corresponds to $\boldsymbol{D(i, j)}$, shown above in orange.

The additional limitation requiring the delivery cost term, $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$, to be "**a function of delivery time required to deliver radiation according to a beam arrangement represented by**" $\boldsymbol{D(i, j)}$, has been largely covered by the discussion of claim 13[a] above. The term $\boldsymbol{S_+}$ in the delivery cost term is given by:

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

(*Id.*)

"$\boldsymbol{(\Delta_+ I)m,n}$ is the change in fluence at the *m*th bixel [i.e., beam element] of the *n*th beam *if positive*." (*Id.* (italics in original).) And this term, when summed over all beams, $\boldsymbol{N_B}$, captures the component of total treatment delivery time that is not fixed. (Webb 2001, N194, N189; Mohan, 1229 (equation 7); Solberg, ¶147)

The "delivery cost term" in Webb 2001 is thus "**a function of delivery time required to deliver radiation**," as claimed. This is further confirmed by the fact that "$\boldsymbol{S_+}$ has dimensions of fluence which <u>scales to monitor units</u>" (Webb 2001, N190), which is a metric used to quantify the delivery time of certain treatment plans. (Solberg, ¶148 (citing '175, 2:28-34; Mohan, 1227 (right column)).)

To the extent Patent Owner argues that "**the delivery cost term [being] a function of delivery time**" requires the *entirety* of the "delivery cost term" to depend on delivery time, this would still be satisfied because a person of ordinary skill would have understood and found it obvious that any of the user-defined weights in $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$, including $\boldsymbol{w_2}$, could be set to zero. (Webb 2001, N190; Solberg, ¶149.) Under the implementation where $\boldsymbol{w_2}$ is set to zero, the delivery cost term simply reduces to $\boldsymbol{w_3[w_1S_+]}$, which takes on the value of $\boldsymbol{S_+}$ multiplied by a constant, $\boldsymbol{w_3w_1}$. (Solberg, ¶149.) As Webb 2001 expressly suggests, setting $\boldsymbol{w_2}$ to zero would allow the user to assign maximum priority to the minimization of treatment time. (Webb 2001, N189; Solberg, ¶150.)

3. Claim 15: "A method as defined in claim 13, wherein the delivery cost term represents at least one of the following: a segment count and an amount of total monitor units, to deliver radiation according to a beam arrangement represented by the respective intensity map."

The delivery cost term in Webb's hybrid cost function represents a **"segment count."** $\boldsymbol{F_{\min}}$ operates to reduce segment count, as explained at length for claim 13[a]. (*See* subsection on "Assignment of $F_{\min}$ based on Complexity.") In short, the value of $\boldsymbol{F_{\min}}$ would generally increase as the size of the segments that would be used for beam delivery increases. (Webb 2001, N190, N194; Solberg, ¶152.) And as the size of component segments increase, the corresponding dose distributions would require fewer segments to deliver, because each segment would deliver a greater quantum of radiation. (Solberg, ¶152.) $\boldsymbol{F_{\min}}$ (more precisely, $\boldsymbol{-F_{\min}}$) thus drives the optimization algorithm towards dose distributions that require fewer segments to deliver.

The delivery cost term in Webb's hybrid cost function also represents **"an amount of total monitor units."** As explained for claim 13[a] and claim 14 above, S_+ captures the non-fixed component of total treatment time as quantified in monitor units, and operates to reduce the amount of total monitor units. (*E.g.*, Webb 2001, N189, N190; Mohan, 1229 (left column), 1227 (right column); Solberg, ¶153.)

C. Prior Art and Date Qualification for Ground 2

Ground 2 builds on Ground 1 by adding Webb 1993, summarized below, and addresses claims 16, 18, and 19.

1. Webb 1993 [Ex 1005]

Webb 1993 is a foundational textbook entitled *The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning*. Webb 1993 qualifies as prior art under §102(b). (Hall-Ellis, ¶¶54-60.)

Webb 1993 provides a definition for "cost function" in its "Glossary of terms" as follows:

> Mathematical function parametrizing the effect of arranging beams in some particular way. For example, a simple cost function could be the RMS difference between the prescribed dose and the delivered dose. More complicated functions could include biological models. The aim of optimization would be to minimize the cost function, possibly

subject to constraints.

(Webb 1993, 344.)

D. Ground 2: Claims 16, 18, 19 Over Webb 2001, Mohan, and Webb 1993

1. Claim 16

As explained for claim 13[a], the "**delivery cost term**" corresponds to the portion of Webb 2001's cost function shown in blue:

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

"intensity map" "delivery cost term"

(Webb 2001, N189.) As further explained, S_+ and $F_{\min}$, independently and as a whole, are a "**function of a number of intensity changes across the respective dose intensity map**," $D(i, j)$. (Solberg, ¶155.)

Claim 16 further recites "**the step of rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value**." This additional limitation would have been obvious over **Webb 2001** and **Mohan** in further combination with **Webb 1993**. To start, Webb 2001 describes a proposal to extend its technique (discussed at length for claim 13 above) to "three-dimensional planning leading to two-dimensional fluence modulations." (Webb 2001, N194.) As explained:

> Instead of creating modulations element-by-element and subsequently interpreting these to leaf movement patterns, an alternative could be to directly create leaf-pattern components which sum to the required modulation. To embody the ideas in this note the technique would include in the cost function a requirement to maximize the sum of the minimum component *field areas*. The requirement to control the monitor-unit efficiency could at the same time be built in by requiring shallow modulations.

(*Id.*)

A person of ordinary skill would have understood and found it obvious that the proposed "requirement to control the monitor-unit efficiency… by *requiring shallow modulations*" would be implemented by subjecting the "**delivery cost term**" of the cost function, $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$, to a maximum-value constraint. **Webb 1993** confirms that the use of constraints in cost functions was a well-known and standard practice. (Webb 1993, 344 (The aim of optimization would be to minimize the cost function, possibly *subject to constraints*.").)

As explained for claim 13[a], the value of $\boldsymbol{S_+}$ captures the component of the total treatment time, as quantified in MUs, that is not fixed. (*E.g.*, Webb 2001, N189, N190; Mohan 1229 (equation 7); Solberg, ¶158.) $\boldsymbol{F_{\min}}$ captures the area or size of the smallest segments used to deliver radiation across the beams. (Webb 2001, N189, N194 ("[I]nclude in the cost function a requirement to maximize the sum of the minimum component *field areas*.") (italics in original).) By setting a constraint on the maximum value of $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$, therefore, all dose distributions that would be delivered by beams whose MUs are excessive in relation to the size of the component segments used would be rejected. (Solberg, ¶158-59.) And in this manner, a requirement on the level "monitor-unit efficiency" and "shallow[ness]" in beam modulation would be enforced. (Webb 2001, N194.)

<u>Rationale and Motivation to Combine</u>: It would have been obvious to combine Webb 2001, Mohan, and Webb 1993. (Solberg, ¶¶160-161.) The combination would have predictably resulted in the optimization process described in Webb 2001, in which dose distributions that would be delivered by beams whose MUs are excessive in relation to the size of the component segments used, and thus produce a value for $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$ that exceeds a user-defined constraint, would be rejected.

Webb 2001, Mohan, and Webb 1993 are all analogous references in the field of intensity modulated radiation therapy. A person of ordinary skill, looking to implement the teachings of Webb 2001 and Mohan, would have naturally consulted Webb 1993 for guidance in doing so. (Solberg, ¶160.)

The motivation to incorporate a constraint on the value of the delivery cost term, $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$, has been discussed above. It provides an advantageous manner of implementing the "requirement to control the monitor-unit efficiency… by requiring shallow modulations" taught by Webb 2001. (Webb 2001, N194; ¶¶161, 158-159.)

2. Claim 18

The limitation of "**wherein the delivery cost term represents total monitor units to deliver the radiation treatment plan**" has been addressed in the analysis of claims 14 and 15 above. As explained for claim 14, the term $\boldsymbol{S_+}$ in Webb 2001's delivery cost term, $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$, captures the non-fixed component of total treatment time as quantified in monitor units. (*E.g.*, Webb 2001, N189, N190; Mohan, 1229 (left column), 1227 (right column); Solberg, ¶163; *compare with*, '175, 2:28-34 ("For some treatment plans… <u>treatment time is controlled by the total radiation beam on time</u> of the linear accelerator used in providing the treatment, <u>which is the Total Monitor Units</u>.").)

The limitation of "**wherein the step of evaluating the objective function includes the step of limiting inflation of total monitor units from initially simple and efficient beam arrangements to more complex beam arrangements**" has been covered in the analysis of claim 16. As explained, Webb 2001 teaches a "requirement to <u>control the monitor-unit efficiency</u>" that would be implemented by persons of ordinary skill by subjecting the "delivery cost term" of the cost function, $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$, to a maximum-value constraint as taught by Webb 1993. (Webb

2001, N194; Webb 1993, 344; ¶Solberg 164.) By constraining the maximum value of $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$, the inflation of $\boldsymbol{S_+}$, which captures the component of total monitor units that is not fixed (*e.g.*, Webb 2001, N189, N190; Mohan, 1229 (left column), 1227 (right column)), is limited as the optimization process proceeds to evaluate different multi-beam arrangements at each iteration. (¶Solberg 164.) In other words, the value of $\boldsymbol{S_+}$ – and likewise the total monitor units that are controlled by $\boldsymbol{S_+}$ – for any beam arrangement evaluated at a particular iteration would not be able to increase beyond a number that would cause $\boldsymbol{w_3[w_1S_+ - w_2F_{min}]}$ to exceed the constraint value.[7]

The combination of Webb 2001, Mohan, and Webb 1993 thus discloses and renders obvious "**wherein the step of evaluating the objective function includes the step of limiting inflation of total monitor units from initially simple and efficient beam arrangements to more complex beam arrangements**." The '175 patent specification confirms that the recitation of progression "from initially simple

[7] As explained for claim 14, it would have been obvious that user-defined weight $\boldsymbol{w_2}$ could be set to zero, in which case $\boldsymbol{S_+}$ (and the total monitor units corresponding to $\boldsymbol{S_+}$) could never exceed the maximum-value constraint divided by the constant $\boldsymbol{w_3w_1}$. (Solberg, ¶164 n.15.)

and efficient beam arrangements to more complex beam arrangements" simply refers to the natural progression of an iterative optimization algorithm such as simulated annealing, which as discussed, is admitted prior art. ('175, 2:64-3:2; Ex. 1012, U.S. 6,038,283, 8:61-65 ("Simulated annealing radiotherapy planning ('SARP') methods are well known in the art…."), 12:34-45.)

To the extent required by the claim, it would have been obvious to implement Webb 2001's hybrid cost function within a simulated annealing optimization process. (Solberg, ¶166.) Simulated annealing was one of a finite number of well-known optimization algorithms for radiotherapy treatment planning, and further provides the well-known benefit of ensuring that evaluated solutions converge to the global minimum of the cost function used. (Solberg, ¶166 (citing Webb 1993, 351).)

3. Claim 19

Independent claim 19 is largely an amalgamation of the limitations recited in claims 13, 15, and 16, addressed above. The analysis provided for those claims is briefly summarized for claim 19 below.

(a) "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:" (Claim 19[preamble])

The preamble of claim 19 is identical to that of claim 13, and thus satisfied by Webb 2001 for the same reasons.

(b) "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, the delivery cost term representing total monitor units to deliver radiation according to a beam arrangement represented by the respective intensity map; and" (Claim 19[a])

"evaluating an objective cost function within an optimizer for each of a plurality of intensity maps": The mapping of the prior art to this limitation is the same as the mapping provided for claim 13[b]'s recitation of "evaluating an objective cost function for each of the plurality of intensity maps." The claimed "**optimizer**" in claim 19[a] corresponds to the same iterative optimization algorithm described in Webb 2001 that was mapped to the "optimizer" recited in claim 13[a]. (Webb 2001, N188.) The "**objective cost function**" corresponds to the same "hybrid cost function" taught by Webb 2001 discussed for claim 13. That equation is again shown below:

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

"intensity map" "delivery cost term"

(Webb 2001, N189.)

<u>"the objective function including a dosimetric cost term and the delivery cost term"</u>: As explained for claim 13[b], the "**dosimetric cost term**" is the term on the left in the equation shown above. The "**delivery cost term**" is the term on the right.

<u>"the delivery cost term representing total monitor units to deliver radiation according to a beam arrangement represented by the respective intensity map"</u>: This limitation has been addressed with respect to claims 13[a] and 15. S_+ captures the non-fixed component of total treatment time as quantified in monitor units, and operates to reduce the amount of total monitor units. (*E.g.*, Webb 2001, N189, N190; Mohan, 129 (left column), 1227 (right column); Solberg, ¶172.)

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

The limitation in claim 19[b] has been addressed with respect to claim 16, and is disclosed and rendered obvious by the combination of Webb 2001, Mohan, and Webb 1993. As explained, Webb 2001 teaches a "requirement to control the monitor-unit efficiency… by requiring shallow modulations" would be implemented by persons of ordinary skill by subjecting the "**delivery cost term**" of the cost function, $\boldsymbol{w_3[w_1S_+ - w_2F_{\min}]}$, to a maximum-value constraint. And this would result in "**rejecting each intensity map resulting in the delivery cost term exceeding a preselected threshold value**." (Solberg, ¶173.)

E. Prior Art and Date Qualification for Grounds 3 and 4

Grounds 3 and 4 address the same claims and cite the same prior art as Grounds 1 and 2, respectively, except Grounds 3 and 4 additionally cite **Siebers** (Ex. 1006) to address potential arguments the Patent Owner may raise with respect to Grounds 1 and 2.

1. Siebers [Ex 1006]

Siebers is an article entitled "Incorporating Multi-leaf Collimator Leaf Sequencing into Iterative IMRT Optimization" from the scientific journal *Medical Physics*. Siebers qualifies as prior art under §102(b). (Hall-Ellis, ¶¶61-66.)

Siebers "propose[s] a simple method to incorporate beam delivery constraints into the IMRT optimization process." (Siebers, 953 (right column).) This optimization process is shown in Figure 2:

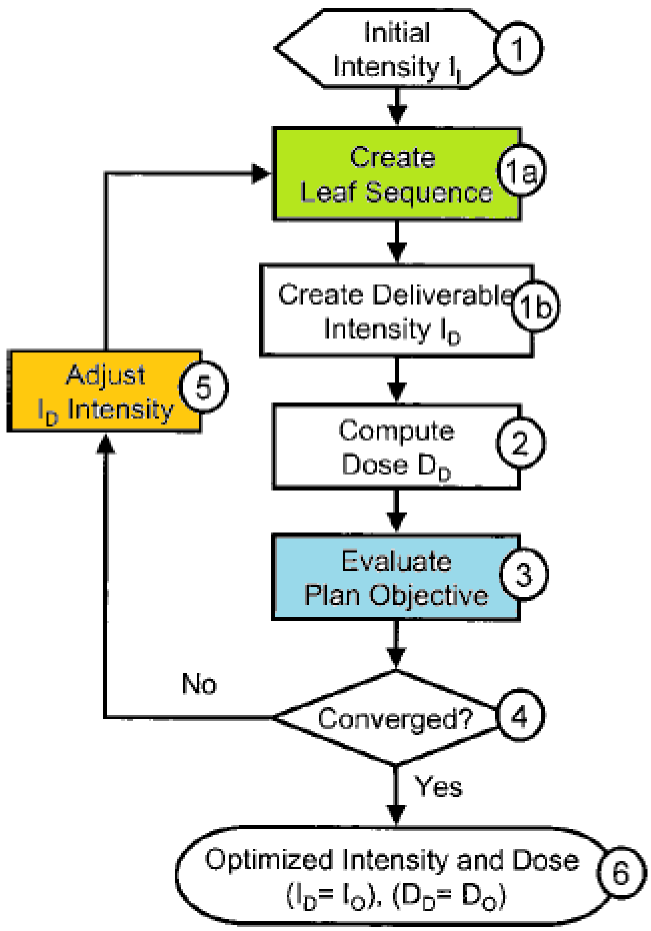


FIG. 2. Flow diagram for the deliverable-based optimization method. Intensities are converted to MLC leaf sequences and deliverable intensities inside of the iterative IMRT optimization loop. The same leaf sequencer is used as in traditional optimization.

(*Id.* (right column) (Fig. 2).) At the beginning of each new iteration, as shown in color annotation above, the optimization algorithm directly creates a leaf sequence based on the input intensity pattern for that iteration.

A. Grounds 3 and 4: Obviousness of Claims 13-15 Over Webb 2001, Mohan, and Siebers (Ground 3) and Claims 16, 18, 19 Over Webb 2001, Mohan, Webb 1993, and Siebers (Ground 4)

Webb 2001 demonstrates how its "hybrid cost function" would operate in the context of a "fairly standard" optimization process, which generates a set of one-dimensional beam profiles (one beam profile for each beam in the multi-beam arrangement) that combine to create a conformal two-dimensional dose distribution for a corresponding "slice" of the three-dimensional target site. (Webb 2001, *e.g.*, N188 ("This is an iterative method which… creates the modulated 1D profiles which, when combined, lead to a conformal 2D dose distribution…. All this is fairly standard…."), N189 ("The *new development* is to compute two extra parameters at each iteration which characterize beam-space and then make use of them in a hybrid cost function.") (italics in original), N194 ("It is not acceptable to simply apply the present technique in two dimensions for each independent dose slice and expect the gains to be unchanged."); Solberg, ¶¶175, 94 n.6.)

Webb 2001 further states:

> The question naturally arises as to how this technique might be extended to three-dimensional planning leading to two-dimensional fluence modulations. This has not been addressed in this note but will be considered for future work. It is not acceptable to simply apply the present technique in two dimensions for each independent dose slice and expect the gains to be unchanged. It is well known that when two-dimensional fluence modulations are passed through so-called interpreters to develop the patterns of leaf movements, it is necessary to take into account the 'hard constraints' of the multileaf collimator such as the need (for some MLCs) to avoid interdigitation and to

> maintain minimum leaf gaps. Hence, in interpreting a series of adjacent one-dimensional fluences created by the technique here, some of the efficiency advantage may be lost.

(Webb 2001, N194.)

Patent Owner may thus attempt argue based on the passage above that a person of ordinary skill would not have been motivated to implement Webb 2001's technique in the context of three-dimensional treatment planning, or that a person of ordinary skill would not have reasonably expected success in applying Webb 2001's technique in the context of three-dimensional planning.

As an initial matter, nothing in the language of the '175 patent claims requires a "three-dimensional" treatment plan that entails multiple "independent dose slices." (Webb 2001, N194.) The claims could be satisfied, for example, by a real-world treatment plan developed according to Webb 2001's teachings to treat a target volume that is "thin" or "shallow" enough to be treated as a single two-dimensional "slice." (Solberg, ¶178.) In fact, Figure 2C of the '175 patent shows the dose distribution of a "clinical treatment plan" with five beams (as indicated by the five "arms" extending outward from the center) and only five total segments ("Segment Count = 5") ('175, 3:31-34), which would have suggested to persons of ordinary skill that the treatment plan depicted could have been developed using an optimization process that treated the target site as a single two-dimensional "slice":

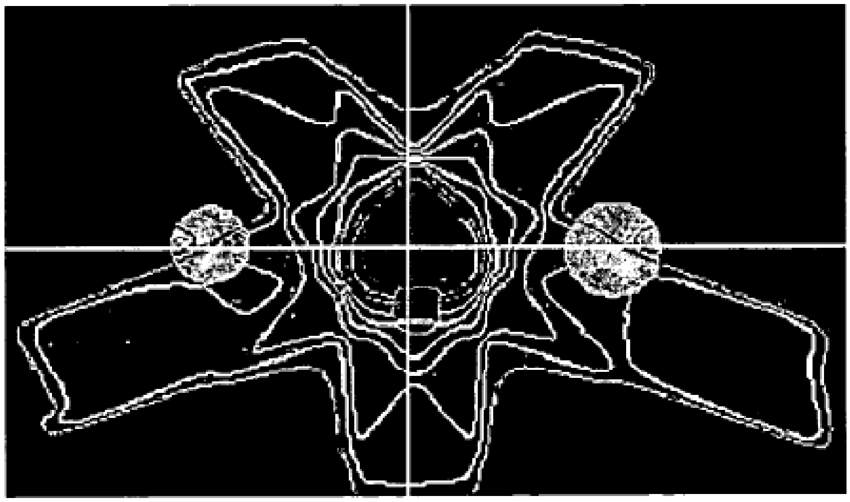


FIG. 2C.

('175, Fig. 2C; Solberg, ¶178.)

In any event, any attempt to rely on the passage from Webb 2001 block-quoted above to show a lack of motivation or reasonable expectation of success would be wholly without merit, as the further combination with **<u>Siebers</u>** (Ex. 1006) will clearly demonstrate, below.

To start, Webb 2001 itself proposed a solution to the question raised "as to how [its] technique might be extended to three-dimensional planning," which would need to "take into account the 'hard constraints' of the multileaf collimator" so as to not lose "some of the efficiency advantage" gained using its hybrid cost function. (Webb 2001, N194.) Webb 2001 explains:

> A possible way forward is the following. Instead of creating modulations element-by-element and subsequently interpreting these to leaf movement patterns, an alternative could be to <u>directly create leaf-pattern components which sum to the required modulation</u>. To

> embody the ideas in this note the technique would include in the cost function a requirement to maximize the sum of the minimum component *field areas*. The requirement to control the monitor-unit efficiency could at the same time be built in by requiring shallow modulations. Done this way, the hard constraints could be directly included by only allowing those leaf-pattern components which satisfied the constraints. Additionally one could build in the transmission effects and head-scatter contribution to dose during the iteration. The field of optimization of IMRT is increasingly moving towards these notions of including all the geometrical and dosimetric features inside the optimization itself.

(Webb 2001, N194.)

Webb 2001 thus proposes that in the context of three-dimensional treatment planning, its hybrid cost function could be used in an optimization process that "directly create leaf-pattern components which sum to the required modulation," which would account for the hard constraints of the MLC because they would be "directly included by only allowing those leaf-pattern components which satisfied the constraints." And this is precisely the optimization technique investigated and experimentally verified in **Siebers**. (Ex. 1006.)

Siebers states: "The objective of this article is to develop a method to incorporate constraints imposed by delivery systems used for intensity modulated radiation therapy (IMRT) into the IMRT treatment plan optimization process."

(Siebers, 952 (left column); *see also id.*, 953 (right column).) This optimization process, which incorporates the constraints of the MLC, is shown in Figure 2:

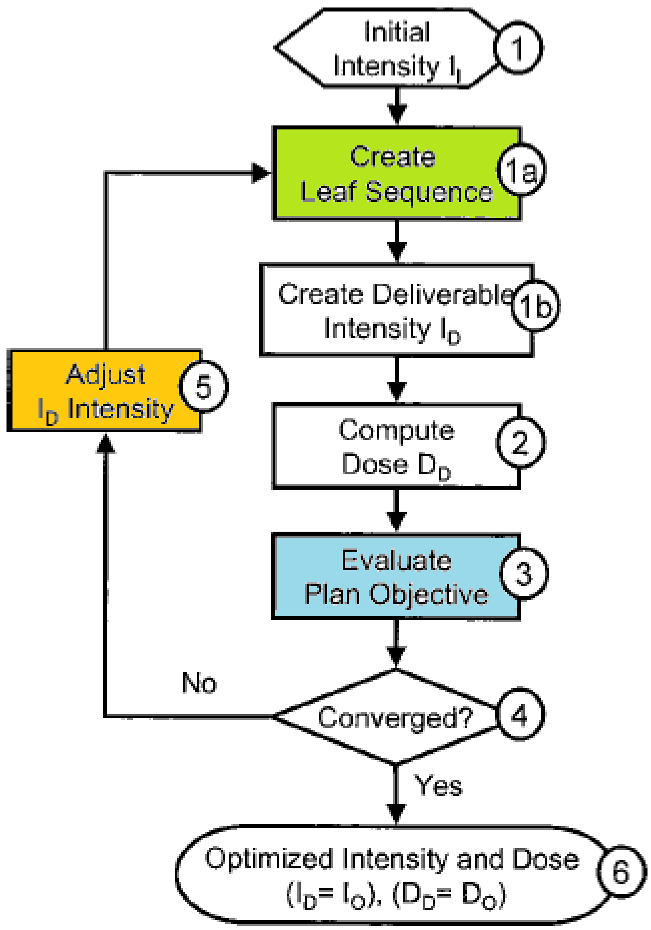


FIG. 2. Flow diagram for the deliverable-based optimization method. Intensities are converted to MLC leaf sequences and deliverable intensities inside of the iterative IMRT optimization loop. The same leaf sequencer is used as in traditional optimization.

(Siebers, 953 (right column) (Fig. 2).)

At the beginning of each new iteration, as shown in color annotation above, the optimization algorithm directly creates the leaf sequence that would sum to the input intensity pattern for that iteration, just as Webb 2001 had proposed. (Solberg, ¶183.) Siebers explains:

> This process is similar to the traditional IMRT optimization flow except that *the computation of leaf sequences* and deliverable intensities *has been moved inside of the optimization loop* immediately prior to the dose computation…. The deliverable intensities (box 1b, Fig. 2) are derived from the MLC trajectories (box 1a, Fig. 2). *They include all restrictions of the MLC delivery* and incorporate the best available approximations related to the transmission and scattering characteristics of the MLC. These deliverable intensities are used to compute the deliverable dose distributions (D_D, box 2, Fig. 2), which are used in turn to evaluate the plan objective function (box 3, Fig. 2), hence, the plan quality score. At the completion of deliverable-based optimization, the optimized solution is, in fact, deliverable to a patient, and dynamic MLC leaf sequences exist. Thus, no further processing or conversions are required. Furthermore, the result is optimal for the constraints and objectives specified.

(Siebers, 955 (left column).)

Under the further combination with Siebers, therefore, the hybrid cost function of Webb 2001 would be adapted to the iterative optimization process detailed in Siebers. Specifically, Webb 2001's hybrid cost function would be evaluated in box 3 of the optimization flow shown in Figure 2 above.

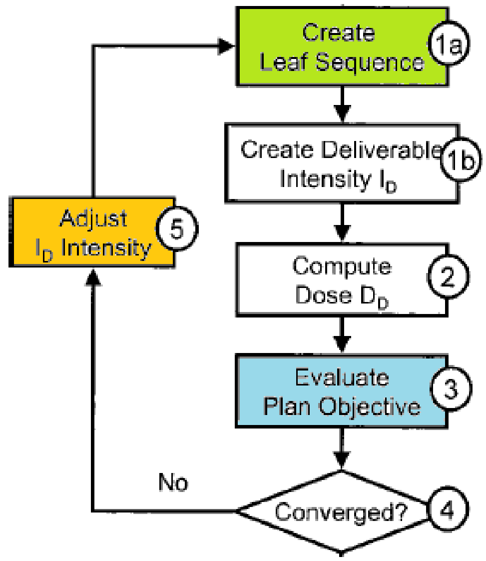
Siebers thus dispels any notion that a person of ordinary would not have been motivated or able to implement Webb 2001's hybrid cost function in the context of three-dimensional treatment planning. (Solberg, ¶185.) Under the further combination with Siebers, Webb 2001's hybrid cost function would provide the same benefits originally detailed in Webb 2001 – providing user control over the tradeoff between dosimetric fitness and delivery efficiency (Webb 2001, *e.g.*, N188) – along with several additional advantages that flow from directly generating leaf sequences within the optimization process, discussed further below.

Siebers also expressly confirms that there would have been no technological obstacle to implementing Webb 2001's hybrid cost function in the context of three-dimensional planning, and a person of ordinary skill would have had every expectation of success. (Solberg, ¶186.) In Siebers, "[t]he deliverable-based optimization method was evaluated by developing alternative treatment plans for 17 IMRT patients." (Siebers, 955 (left column) – 955 (right column); *see also id.*, 952 (Abstract).) And the experimental results demonstrate overall success:

> Compared with standard optimization plus conversion to deliverable beams, deliverable-based optimization results show improved isodose coverage and a reduced dose to critical structures. Deliverable-based optimization results are close to the original nondeliverable optimization results, suggesting that IMRT can overcome the MLC limitations by adjusting individual beamlets.

(Siebers, Abstract; *see also id.,* 956 (left column), 957 (right column), 958 (right column) .)

Rationale and Motivation to Combine: It would have been obvious to further combine the Ground 1 and Ground 2 references, including Webb 2001, with Siebers. (Solberg, ¶¶188-195.) The combination would have predictably resulted in the hybrid cost function technique for providing control of a trade-off between delivery efficiency and dosimetric fitness, as disclosed in Webb 2001, in which the hybrid cost function is adapted to the optimization process detailed in Siebers. (*E.g.*, Webb 2001, N189 (equation 2); Siebers, 953 (Figure 2) (partially shown at above right), 955.) Accordingly, the optimization process at the beginning of each new iteration would directly create the leaf sequence that would sum to the input intensity pattern for that iteration, and thereby account for the constraints of the MLC. (Siebers, 953 (Figure 2, blocks 5 and 1a), 955 (left column); *compare with*, Webb 2001, N194.) And thereafter, the dose distribution that would result from the generated leaf sequence would be evaluated using the hybrid cost function adapted from Webb 2001.



(Siebers, 953 (Figure 2, block 3).)[8]

Webb 2001, Mohan, Webb 1993, and Siebers are all analogous references in the field of intensity modulated radiation therapy (IMRT). A person of ordinary skill, looking to implement the teachings on IMRT described in Webb 2001, Mohan, and Webb 1993 would have naturally consulted Siebers for guidance in doing so. (Solberg, ¶189.) And a person of ordinary skill would have had every expectation that the combination would be successful. (Solberg, ¶¶185-186, 195.)

In fact, Siebers specifically credits the Webb 2001 paper for the "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." (Siebers, 953 (left column).) Siebers also implements the leaf sequence generator process described in the Mohan reference. (Siebers, 954 (right column).) The close collaboration exhibited in the field of IMRT, and the closely analogous nature of the references, would themselves have provided suggestions to combine. (Solberg, ¶190.)

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[8] A person of ordinary skill would have possessed the capability and creativity to adapt the precise formulation of the hybrid cost function to the extent needed to evaluate three-dimensional dose distributions. (Solberg, ¶188 n.16.)

A person of ordinary skill would have been motivated to look to Siebers, moreover, because it provides the specific implementation details and experimental data on the solution for three-dimensional planning proposed in Webb 2001. (Webb 2001, N194.) Webb 2001 and Siebers both identified some of the same problems posed by MLC constraints when generating leaf patterns for beam delivery. (*Compare* Webb 2001, N194; *with* Siebers, 952 (right column).)

Both references also proposed the same solution – to include MLC constraints as part of optimization by generating leaf patterns for beam delivery directly within the optimization process. (*Compare* Webb 2001, N194; *with* Siebers, *e.g.*, 952 (left column).) While Webb 2001 left the investigation into this solution "for future work" (Webb 2001, N194), Siebers performed the actual work and evaluated its effectiveness using experimental data. (Siebers, *e.g.*, 952 (Abstract).)

As mentioned, the hybrid cost function, when adapted to the optimization process detailed in Siebers, would provide the same benefits originally detailed in Webb 2001 – providing user control over the tradeoff between dosimetric fitness and delivery efficiency (Webb 2001, *e.g.*, N188) – along with several other benefits that flow from directly generating leaf sequences within the optimization process. (Solberg, ¶193.) This includes the ability to account for transmission effects and the contribution of scatter radiation to the delivered dose. (Webb 2001, N194; Siebers, 955 (left column).) It may also "reduce the need for empirical adjustment of objective function parameters and reoptimization of a plan to achieve desired results." (Siebers, 952 (Abstract).) Ultimately, it would likely result in a better treatment plan. (Siebers, 952 (right column) – 953 (left column).)

A person of ordinary skill would therefore have had no shortage of motivations – many of them expressly taught – to further combine with Siebers. (Solberg, ¶194.) Beyond the technical advantages discussed at length above, a person of ordinary skill would have been motivated to look to Siebers because as noted in Webb 2001, "[t]he field of optimization of IMRT [was] increasingly moving towards these notions of including all the geometrical and dosimetric features inside the optimization itself." (Webb 2001, N194.)

IX. CONCLUSION

Petitioner respectfully requests institution of review on the challenged claims.

Dated: October 17, 2019

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE WITH WORD COUNT

Pursuant to 37 C.F.R. § 42.24(d), I certify that this petition complies with the type-volume limits of 37 C.F.R. § 42.24(a)(1)(i) because it contains 13,897 words, according to the word-processing system used to prepare this petition, excluding the parts of this petition that are exempted by 37 C.F.R. § 42.24(a) (including the table of contents, a table of authorities, mandatory notices, a certificate of service or this certificate word count, appendix of exhibits, and claim listings).

DATED: October 17, 2019

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CERTIFICATE OF SERVICE

I hereby certify, pursuant to 37 C.F.R. Sections 42.6 and 42.105, that a complete copy of the attached **PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 7,266,175,** including all exhibits (**Nos. 1001-1015**) and related documents, are being served via Federal Express on the 17th day of October, 2019, the same day as the filing of the above-identified document in the United States Patent and Trademark Office/Patent Trial and Appeal Board, upon Patent Owner by serving the correspondence address of record with the USPTO as follows:

Best Medical International, Inc.
Patent Counsel
7643 Fullerton Road
Springfield, VA 22153

And, via Federal Express upon counsel of record for Patent Owner in the litigation pending before the U.S. District Court for the District of Delaware entitled *Best Medical Int'l, Inc. v. Varian Medical Systems, Inc.*, Case No. 1:18-cv-01599-UNA as follows:

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