UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELEKTA INC.,
Petitioner

v.

BEST MEDICAL INTERNATIONAL, INC.,
Patent Owner.

Case No.: IPR2020-00956

U.S. Patent No. 7,015,490

# PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 7,015,490

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## LIST OF EXHIBITS

| Exhibit | Description |
|---|---|
| **1001** | U.S. Patent No. 7,015,490 B2 to Duan Qiang Wang, *et al*. (filed August 11, 2004, issued March 21, 2006) ("'490" or "'490 patent") |
| **1002** | Declaration of Timothy D. Solberg, Ph.D. ("Solberg") |
| **1003** | U.S. Patent Application Publication No. 2003/0086530 ("Otto") |
| **1004** | U.S. Patent No. 6,853,705 to Sha Chang (filed March 28, 2003, issued February 8, 2005) ("Chang") |
| **1005** | "*The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning*" ("Webb") |
| **1006** | "The Impact of Fluctuations on Intensity Patterns on the Number of Monitor Units and the Quality and Accuracy of Intensity Modulated Radiotherapy," *Medical Physics* ("Mohan") |
| **1007** | Provisional U.S. Application 60/487,067 |
| **1008** | Carol, M.P., Chapter 2 - IMRT: Where We Are Today, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 17-36 ("Carol-2") |
| **1009** | U.S. Patent 5,596,619 ("'619 or '619 Patent") |
| **1010** | U.S. Patent 5,802,136 ("'136 or '136 Patent") |
| **1011** | Declaration of Sylvia Hall-Ellis, Ph.D. |
| **1012** | U.S. Patent 6,038,283 ("'283 or '283 Patent") |
| **1013** | *Webster's Third New International Dictionary, Unabridged* (2002) |
| **1014** | Declaration of Mark P. Carol submitted re U.S. Appl. No. 10/887,966, dated January 2007 ("Carol Decl.") |

Elekta Inc. ("Elekta" or "Petitioner") respectfully submits this petition for *Inter Partes* Review of claims 1, 4, 17, 18 and 19 of U.S. Patent No. 7,015,490 (Ex. 1001) ("the '490 patent"). The Board previously instituted review of these claims based on the petition filed by *Varian Medical Systems, Inc.* ("Varian") in IPR2020-00076. The challenges to claims 1, 4, 17, 18 and 19 presented herein are substantively identical to Varian's challenges in IPR2020-00076 and are based on the same evidence as presented in IPR2020-00076, as further explained in the motion for joinder submitted with this petition.

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

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

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

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

Patent Owner asserted the '490 patent in *Best Medical International, Inc.* v. *Elekta Inc. and Elekta Limited*, Civil Action 1:19-cv-03409-MLB (currently pending in the Northern District of Georgia, and previously pending in the District of Delaware as Civil Action No. 1:18-cv-01600-MN) and *Best Medical International,* *Inc*. v. *Varian Medical Systems, Inc. et al*, Civil Action 1:18-cv-01599 (currently pending in the District of Delaware).

The '490 patent was challenged in *Elekta Inc. v. Best Medical International, Inc.,* IPR2020-00067, filed October 18, 2019, for which institution was denied on April 24, 2020; and *Varian Medical Systems, Inc., v. Best Medical International, Inc.,* IPR2020-00076, filed October 18, 2019. Based upon the latter Varian Petition, the Board instituted review of claims 1, 4, 17, 18 and 19 on April 24, 2020.

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

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

Pursuant to 37 C.F.R. §42.10(b), concurrently filed with this Petition is a Power of Attorney executed by Petitioner and appointing the above counsel.

### D. Service Information

Postal mailings and hand-deliveries for lead and back-up counsel should be addressed to: Tamara D. Fraizer, Squire Patton Boggs (US) LLP, 1801 Page Mill Road, Suite 110, Palo Alto, CA 94304-1043 (Telephone: (650) 843-3201; Fax: (650) 843-8777). Pursuant to 37 C.F.R. §42.8(b)(4), Petitioner consents to e-mail service at: tamara.fraizer@squirepb.com; sfripdocket@squirepb.com.

## II. FEE PAYMENT

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

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

### A. Grounds for Standing

The Petitioner certifies that the ’490 patent is available for *inter partes* review, and that the Petitioner is not barred or otherwise estopped.

### B. Identification of Challenge and Statement of Precise Relief Requested

Petitioner requests institution of IPR based on:

| Ground | Claims | Basis for Challenge under §103(a) |
|---|---|---|
| 1 | 1, 4, 17-19 | Otto (Ex. 1003), Chang (Ex. 1004), Webb (Ex. 1005), Mohan (Ex. 1006) |

Submitted with this Petition is the Declaration of Dr. Timothy Solberg (Ex. 1002), a qualified expert. (Solberg, ¶¶1-9, Ex. A.)

### C. Considerations Under § 325(d) and §314(a)

The sole ground proposed in this Petition relies on the combination of Otto, Chang, Webb, and Mohan. Webb and Mohan were not cited during prosecution of the ’490 patent. Otto was identified by the applicant in the file history of the ’490 patent and the publication of the application that became Chang was also referenced in the file history. However, neither Otto nor Chang were substantively discussed (and, in fact, no rejections were issued by the Examiner prior to allowance). Additionally, there is no evidence that the Examiner ever evaluated Otto in combination with Chang; and, further, because Webb and Mohan were not before the Examiner, the Examiner did not evaluate the proposed combination of Otto, Chang, Webb, and Mohan. Therefore, this Petition does not present a situation in which "the same or substantially the same prior art or arguments previously were presented to the Office" under §325(d).

## IV. LEVEL OF ORDINARY SKILL IN THE ART

A person of ordinary skill in the art as of August 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 '490 patent, reproduced in condensed form below. (Solberg, ¶¶24-33.)

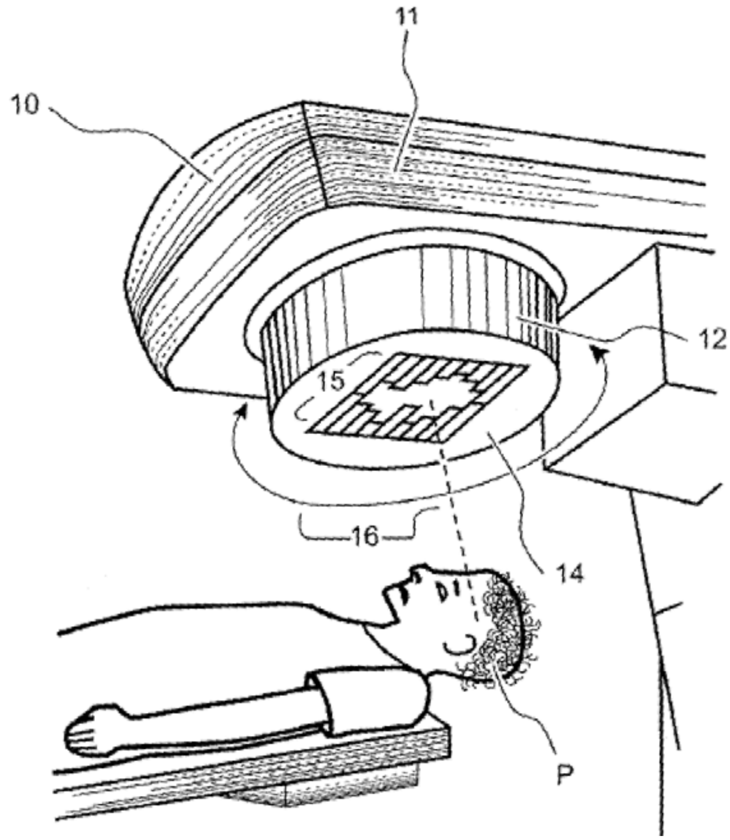
### A. Multileaf Collimators (MLCs) and Their Use in Intensity Modulated Radiation Therapy

As explained in the "Background" section of Otto:

> In radiation therapy a radiotherapy device is used to generate a source of radiation for the treatment of patients. The device may comprise a linear accelerator, for example. A typical radiotherapy device is mounted on a rotating gantry that allows radiation beams focused on a target to intersect the patient at varying orientations. Radiation to healthy tissue and organs must be restricted to avoid detrimental effects to the patient. The amount of radiation that can be concentrated on the target is limited by the need to limit the radiation dosage received by normal tissue surrounding the target.

(Otto, ¶0003.)

To limit radiation received by normal tissue surrounding a tumor target, a multileaf collimator, or "MLC," is commonly used as a beam-shielding device. Otto provides a figure showing an MLC (indicated by numeral 14):




(Otto, Fig. 1.)

As explained in Otto:

> A beam-shielding device modifies the spatial distribution of the radiation beam by selectively blocking areas where lower amounts of radiation are desired. A multileaf collimator is commonly provided in the path of the radiation beam for this purpose. The multileaf collimator shapes the radiation beam. The multileaf collimator has two opposing banks of adjacent blocking leaves. The leaves can each be moved in and out of the radiation beam to define arbitrary field shapes. The multileaf collimator can be used to shape the radiation beam so that it roughly matches the shape of the target area.

(Otto, ¶0004.)

Moreover, because the leaf pairs of the MLC can be moved to form different configurations that shape the beam in different ways, MLCs are commonly used to create an "intensity modulated" radiation field, where different points in the field can receive different levels of radiation intensity. (Solberg, ¶28.)

### B. Optimization of Collimator Angle

Because of the physical limitations of the MLC (*e.g.*, each leaf pair must have a certain width), the MLC leaves cannot always conform perfectly to the desired target area for receiving radiation. (Solberg, ¶29.) This is shown in Figure 5.17 from the 1993 Webb textbook:

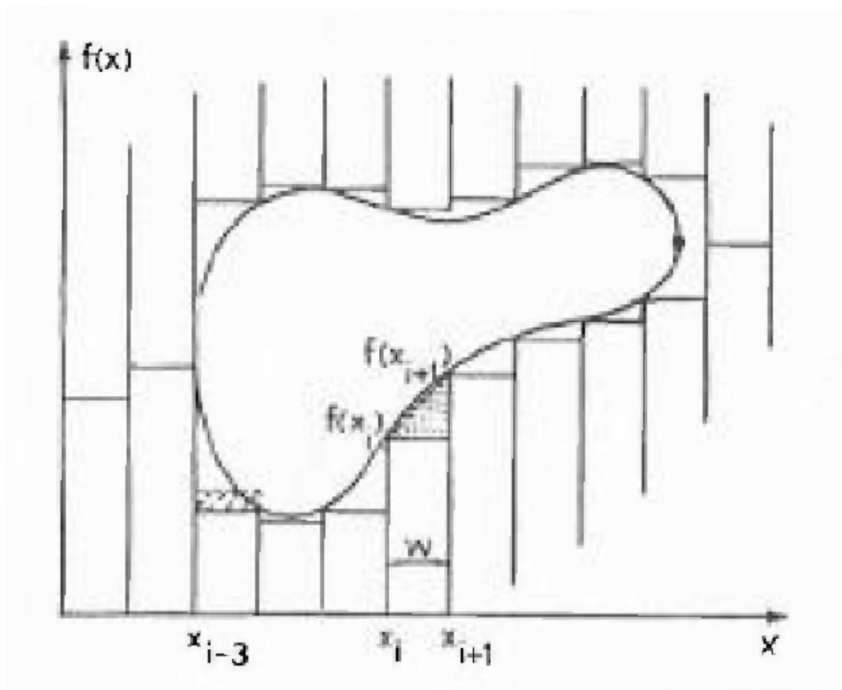



**Figure 5.17.** ***Showing the fitting of a planar target area with a multileaf collimator. The dotted area is the excess region treated by the i th leaf. The best orientation of the leaves relative to the area is that which minimizes the sum of such dotted areas of excess. (From Brahme (1988).)***

(Webb, 233 (Fig. 5.17).)

Accordingly, to optimize the conformity of the MLC to a radiation target, it was well-known that the collimator should be oriented so as to minimize the area seen in the beam's-eye-view of normal tissue outside the target volume. (Solberg, ¶30 (citing Webb, 233-235).) This technique was known as "Brahme's Theory of Orientation," and dates back to a paper authored by Brahme in 1988.

Otto provides a figure that shows how the collimator can be rotated to define different areas as "seen" in the beam-eye-view:

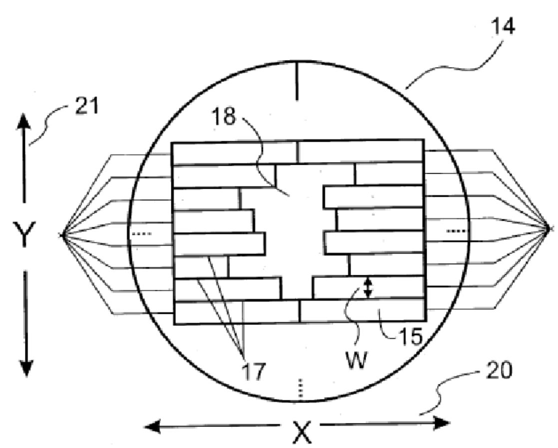



FIGURE 2A

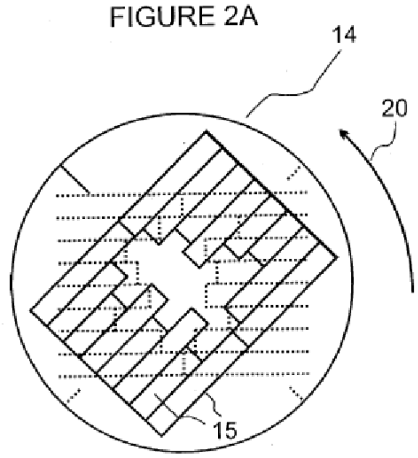



FIGURE 2B

(Otto, Figs. 2A, 2B.) As shown, the areas not covered by MLC leaves would receive radiation generated by the radiation source (*e.g.*, linear accelerator), whereas the areas covered by the MLC leaves would be blocked from receiving radiation.

### C. The Use of Cost Functions in Optimization

As shown above, beam-shielding devices such as MLCs enable treatment beams to be arranged in many different ways, depending on a multiplicity of parameters capable of being varied, such as the position of the leaves and the orientation of the collimator angle. To assist a treatment planner in identifying the best way to arrange beams to fulfill a desired objective, computer-based optimization algorithms are commonly used. (Solberg, ¶32.) In the context of computer-based optimization, a standard technique is to use what is known as a "cost function," which is a mathematical function that quantifies the effect of arranging beams in different ways by distilling the desirability or optimality of the different options available down to a single value. (*Id*.) As explained in the definition for "cost function" provided in the 1993 Webb textbook:

> **COST FUNCTION**: 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, 344.)

For a given cost function, therefore, the optimal arrangement corresponds to when the value of the cost function has reached its minimum. (Solberg, ¶33.)

## VI. SUMMARY OF THE ’490 PATENT

The ’490 patent is entitled “Method and Apparatus For Optimization of Collimator Angles in Intensity Modulated Radiation Therapy Treatment,” and relates to “a method and apparatus for optimization of collimator angles for multileaf collimators (“MLC”) used in intensity modulated radiation therapy treatment.” (’490, 1:29-31.)

The ’490 patent states that “[w]hen determining collimator angles in intensity modulated radiation therapy treatment... (‘IMRT’) inverse treatment plans for use with a MLC radiation delivery system, the most common practice currently is to select collimator rotation angles so that the MLC can be best conformed to the shape of the target, or lesion, in the radiation beam’s eye view.” (’490, 1:33-39.) The ’490 patent admits, as mentioned above, that this known practice is “based upon Brahme’s orientation theory, by which the conformity for targets is prioritized.” (’490, 1:40¬44.)

The ’490 patent asserts that in prior art techniques for selecting a collimator rotation angle, “no consideration is given to delivery efficiency, *e.g.*, reduction of the number of segments and monitor units (‘MU’).” (’490, 1:40-44; *see also id.*, 1:52-56.) The ’490 patent thus purports to disclose “a new algorithm to determine collimator angles in favoring, or enhancing, IMRT radiation therapy treatment plan delivery efficiency.” (’490, 2:2-4.)

## VII. CLAIM CONSTRUCTION

Petitioner does not believe any claim terms require express construction from the Board at this time.

## VIII. THE CHALLENGED CLAIMS ARE UNPATENTABLE

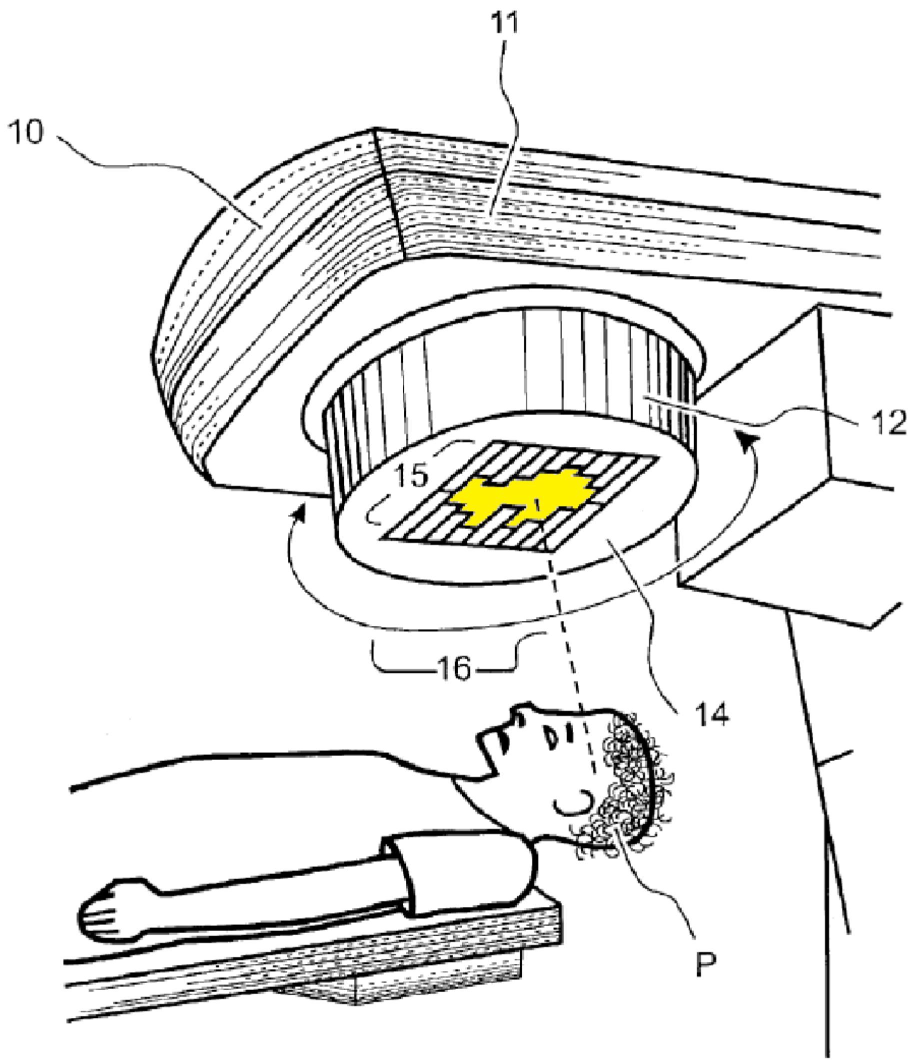
This Petition presents a single Ground of obviousness for claims 1, 4, and 17-19, based on the combination of Otto, Chang, Webb, and Mohan.

### A. Prior Art and Date Qualification

#### 1. Otto [Ex. 1003]

**Otto**, U.S. Patent Application Publication No. 2003/0086530, entitled “Methods and Apparatus for Planning and Delivering Intensity Modulated Radiation Fields with a Rotating Multileaf Collimator,” relates to “the delivery of radiotherapy by way of a radiotherapy device equipped with a multi-leaf collimator.” (Otto, ¶0002.). Otto qualifies as prior art under §§102(a) and 102(e).

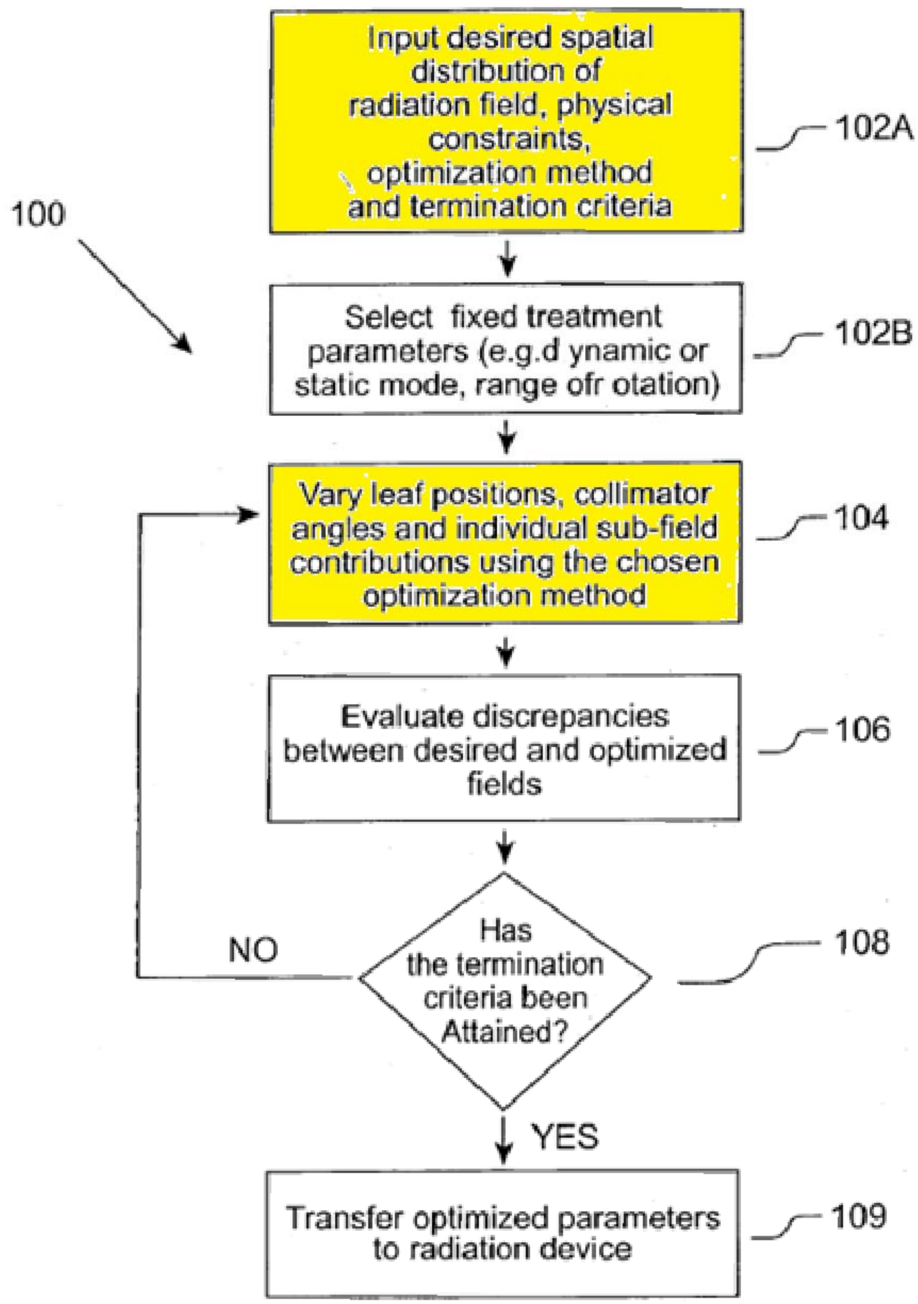
Otto’s radiotherapy device, which includes an MLC, is shown below:




(Otto, Fig. 1.)[1] As shown, the radiation beam is delivered through the opening of the MLC (shown in yellow) to the radiation target.

Otto describes an optimization process for determining the parameters of the MLC for delivering a desired radiation field:

[1] All emphasis and color annotation has been added unless otherwise noted.




(Otto, Fig. 5.) The optimization process varies the parameters of the MLC until a set of optimized parameters are determined (*e.g.*, block 109). As shown in block 104, among the parameters that can be varied are the leaf positions and collimator angles. Further details about Otto are provided in the analysis of the claims below.

### 2. Chang [Ex. 1004]

**Chang**, U.S. Patent No. 6,853,705, entitled "Residual Map Segmentation Method for Multi-Leaf Collimator-Intensity Modulated Radiotherapy," "relates to the optimized configuration of multi-leaf collimator leaves for delivery of IMRT." (Chang, 1:9-10.) Chang qualifies as prior art under §102(e).

Chang emphasizes the benefits of optimizing the orientation of the collimator, teaching that it "can have a considerable influence on the quality and efficiency of the treatment":

> For discrete MLC-IMRT techniques, the orientation of the MLC leaves can have a considerable influence on the quality and efficiency of the treatment. The present method also recognizes that MLC leaves can be translated to any position within their operating range to a great degree of accuracy (i.e., micro-scale). As indicated hereinabove, previous methods have not taken advantage of the continuous positioning capability of the MLC hardware of commercially available medical LINAC systems, but rather position MLC leaves by indexing them in 1-cm increments. The present method, on the other hand, takes full advantage of both the continuous MLC leaf positioning and the continuous collimator angle selection available in MLC-equipped radiotherapy machines. Optimization of collimator orientation assists in generating a more accurate intensity map with less required segment fields.

(Chang, 9:52-67 (underlining added).)

Petitioner cites Chang for its teaching that an optimal collimator rotation angle can be chosen to fulfill the dual objectives of (1) "find[ing] the collimator angle that conforms to the contour as closely as possible" (Chang, 10:34-36, Fig. 8A, Fig. 8B), while (2) factoring in "the influence of such solution... on treatment delivery efficiency" (Chang, 11:10-12). Chang thus shows that the '490 patent's claim that in prior art techniques "by which the conformity for targets is prioritized," "no consideration is given to delivery efficiency," is inaccurate. ('490, 1:40-44.)

### 3. Webb [Ex. 1005]

**Webb** is a foundational textbook entitled "*The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning*." Webb qualifies as prior art under §102(b). (Ex. 1011, Hall-Ellis, ¶¶48-54.)

As its title suggests, Webb teaches the foundational principles of radiation therapy. As mentioned, Webb provides a definition for "cost function" in its "Glossary of Terms" that shows cost functions were a standard and foundational technique used in the optimization of treatment beams:

> **COST FUNCTION**: 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, 344.). Webb also describes "Brahme's Theory of Orientation," previously mentioned.

### 4. Mohan [Ex. 1006]

**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). (Ex. 1011, Hall-Ellis, ¶¶42-47.)

The stated purpose of Mohan "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, Abstract.) Mohan is cited for its description of a known mathematical function for determining the minimum number of MUs, also referred to as "beam-on time," required to deliver a given radiation field from a particular direction of leaf travel. (Mohan, *e.g.*, 1227 (right column).) That function, as it applies to a particular leaf pair, 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).)

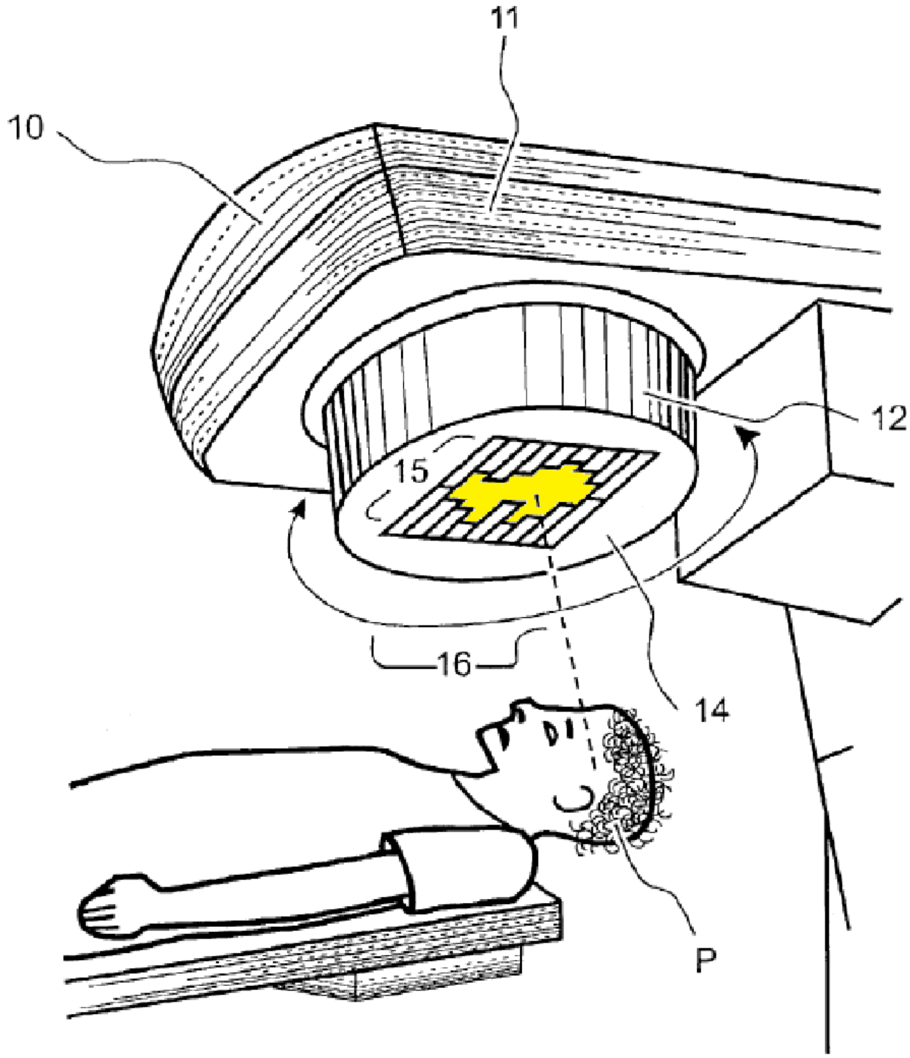
The function above demonstrates that "the beam-on time will increase depending upon both the frequency and the amplitude of the fluctuations." (Mohan, 1229 (left column).) Mohan further teaches "optimiz[ing] the collimator angle for each beam in order to find orientations which minimize fluctuations." (Mohan, 1237 (left column).)

### B. Ground 1: Claims 1, 4, and 17-19 Over Otto, Chang, Webb, and Mohan

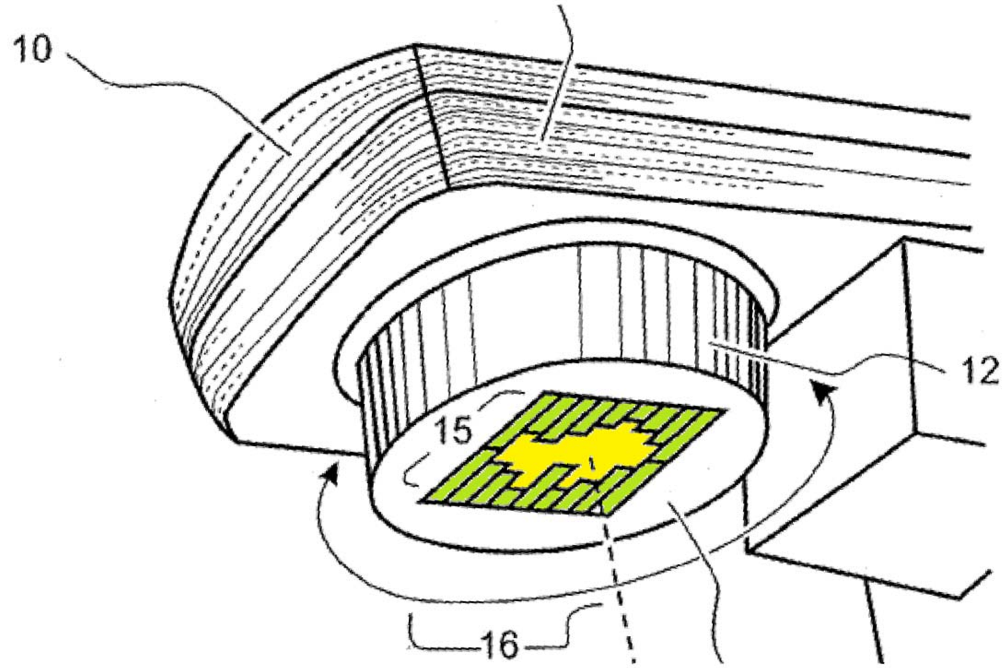
#### 1. Claim 1: "A computer-implemented method of determining a collimator angle of a multi-leaf collimator having an opening and a plurality of multi-leaf collimator leaf pairs for closing portions of the opening to form a radiation beam arrangement having a plurality of radiation beam segments to apply radiation to a tumor target, the method comprising the steps of:" ([preamble])

To the extent the preamble of claim 1 is limiting, it is fully disclosed and rendered obvious by **Otto**.

"a multi-leaf collimator having an opening and a plurality of multi-leaf collimator leaf pairs": Figure 1 shows the radiotherapy device in Otto:




(Otto, Fig. 1.) The "**multi-leaf collimator**" of the radiotherapy device is indicated by numeral 14. (Otto, *e.g.*, ¶0025.) The MLC has an "**opening**" as annotated in yellow. (Otto, *e.g.*, ¶¶0009, 0004.) The MLC also has "**a plurality of multi-leaf collimator leaf pairs**." (Otto, *e.g.*, ¶¶0004 ("The multileaf collimator has two opposing banks of adjacent blocking leaves."), 0041.) The MLC leaf pairs are indicated by numeral 15 in Figure 1 (Otto, *e.g.*, ¶¶0025, 0026), and annotated in green below:




(Otto, Fig. 1 (partial figure).)

MLC with leaf pairs "for closing portions of the opening to form a radiation beam arrangement having a plurality of radiation beam segments to apply radiation to a tumor target": Otto explains that the leaf pairs of the MLC are "**for closing portions of the opening to form a radiation beam arrangement having a plurality of radiation beam segments to apply radiation to a tumor target**":

> The multileaf collimator shapes the radiation beam. The multileaf collimator has two opposing banks of adjacent blocking leaves. The leaves can each be moved in and out of the radiation beam to define arbitrary field shapes. The multileaf collimator can be used to shape the radiation beam so that it roughly matches the shape of the target area.

> A method known as <u>intensity modulation may be used to tailor a radiation field</u> to further reduce the amount of radiation received by healthy tissue. This method <u>provides a radiation field which has a non-uniform intensity over its spatial extent</u>. A complete treatment may comprise the delivery of an [sic] different <u>intensity modulated radiation field</u> from each of a plurality of gantry angles.
>
> <u>A non-uniform field may be delivered by delivering radiation in each of a set of uniform sub-fields, each having a different multileaf collimator configuration</u>. Intensity modulated fields may be delivered using static or dynamic methods. In static methods each sub-field is shaped while the radiation beam is off and then a radiation sub-field is delivered once the leaves are in position. In dynamic methods the leaves are moved while the beam is on.

(Otto, ¶¶0004-0006.)

As explained, the MLC leaf pairs "**clos[e] portions of the [MLC] opening**." (Otto, ¶0004 ("The leaves can each be moved in and out of the radiation beam to define arbitrary field shapes.").) And for purposes of applying Otto to claim 1, the "**radiation beam arrangement**" takes the form of a beam arrangement formed by the MLC leaves to deliver an "intensity modulated radiation field" from a particular gantry angle, i.e., "a radiation field which has a non-uniform intensity over its spatial extent." (Otto, ¶0005.)[2] As the block-quoted passage makes clear, such a non-uniform field may be delivered using a set of "different [MLC] configurations." (Otto, ¶0006.)

In other words:

> The radiation passes through collimator 12 and is shaped by multileaf collimator 14. The shaped radiation impinges onto the patient P. The total radiation dosage delivered at a point in the patient from several sub fields is the sum of the radiation dosage delivered by each sub field individually. Therefore a radiation field which closely approximates an ideal radiation field can be delivered by delivering several appropriately configured sub-fields at different times.

(Otto, ¶0027.)

Otto thus teaches a particular "**radiation beam arrangement**," i.e., a beam arrangement that gives rise to a non-uniform or "intensity modulated" radiation field, that includes "**a plurality of radiation beam segments**," i.e., a sequence of distinct MLC leaf shapes or configurations used to deliver the radiation. (Solberg, ¶61.) Petitioner's mapping of the prior art relies on the "dynamic" delivery method, in

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[2] The '490 specification confirms that the claimed method of "**determining a collimator angle**" can apply to a single beam delivered from a particular gantry angle, and thus the recited "**radiation beam arrangement**" can refer to the arrangement of just one beam. ('490, 10:2-6, 3:53-57.)

which "the leaves are moved while the beam is on." (Otto, ¶0006.) This is the "dynamic MLC delivery" disclosed in the '490 patent. ('490, 9:54-59.)

"[a] computer-implemented method of determining a collimator angle" of the MLC: As explained, "[t]he [MLC] leaves can each be moved in and out of the radiation beam to define arbitrary field shapes." (Otto, ¶0004.) Otto discloses that in addition to leaf positions, the **collimator angle** can be varied to provide different field shapes for radiation. (Otto, *e.g.*, ¶¶0025, 0026 ("Radiotherapy device 10 comprises a control system which is coupled to control mechanisms which move leaves 15 and rotate multi-leaf collimator 14.").) This is shown in Figures 2A and 2B, which depict two exemplary MLC configurations that have different collimator angles (Otto, ¶¶0018, 0028):

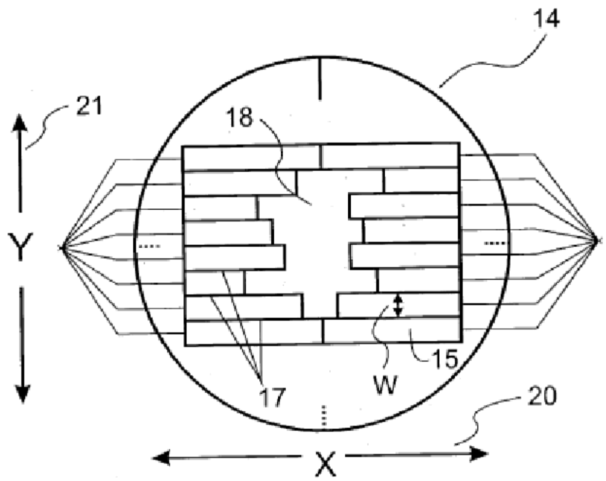



FIGURE 2A

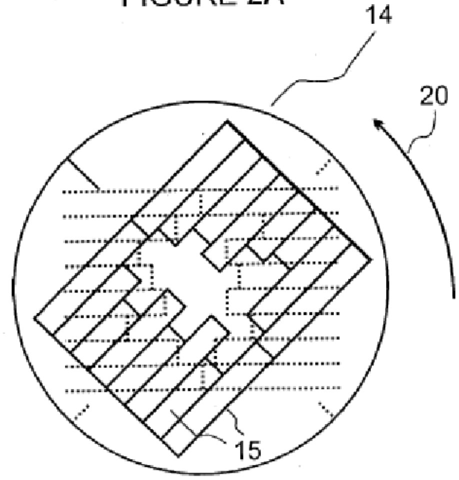



FIGURE 2B

(Otto, Figs. 2A, 2B.) For purposes of ensuring clarity, Dr. Solberg has explained how the concept of a "collimator angle" is distinct from "gantry angle." (Solberg, ¶63.)

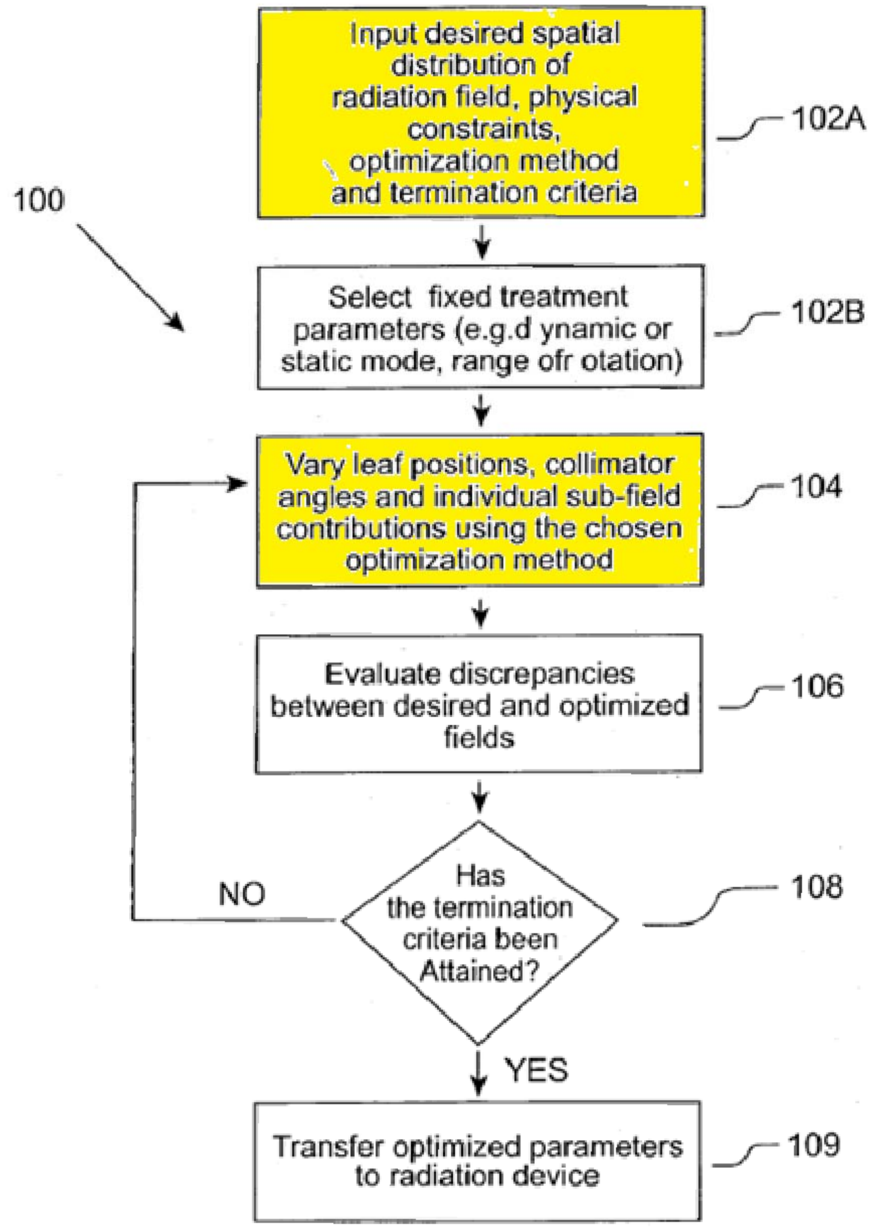
Otto discloses that for a desired radiation field to be delivered, in one embodiment, the appropriate **collimator angle** is first **determined** as part of a **computer-implemented** optimization process that generates the sequence of MLC configurations to be used. (Otto, *e.g.*, ¶¶0044 ("[A] method 100 which may be used to identify a set of sub-fields which will produce a desired overall radiation field. Method 100 may be performed on a treatment planning computer system....”), 0053 (“Block 104 determines a set of configurations for delivering a number of sub-fields. Each configuration specifies leaf positions, collimator angles and sub-field contributions. All the parameters that are not fixed may be varied according to the chosen optimization method.”), 0056 (“If... the termination criteria has been attained then configuration information including leaf positions, collimator angles and individual sub-field contributions is stored or transferred to radiation device 10 for patient treatment.”), 0060-0064, Fig. 5, Fig. 6.)

Further details about Otto’s optimization process and how it determines the appropriate collimator angle are discussed further below.

#### (a) “calculating an initial radiation beam arrangement according to a desired prescription; and” (1[a])

Claim 1[a] is disclosed and rendered obvious by **Otto** in view of **Chang**. Otto discloses an optimization process that includes the step of “**calculating an initial radiation beam arrangement according to a desired prescription**,” and Chang is cited for its implementation details.

Otto’s optimization process is shown in Figure 5 (Otto, ¶¶0021, 0044):




(Otto, Fig. 5.)

As shown, the "**desired prescription**" is input into Otto's optimization flow in block 102A: "In block 102 the desired overall radiation field is provided. The desired overall radiation field may be specified in output from treatment planning software." (Otto, ¶0044.) The '490 specification confirms that the "**desired**

**prescription**," as claimed, can refer to the desired radiation to be delivered. ('490, 4:35-38; Solberg, ¶68.)[3]

Otto explains that after the desired radiation field is input in block 102:

> Block 104 determines a set of configurations for delivering a number of sub-fields. Each configuration specifies leaf positions, collimator angles and sub-field contributions. All the parameters that are not fixed may be varied according to the chosen optimization method.

(Otto, ¶0053.)

A person of ordinary skill would have understood and found it obvious that as part of the "optimization method" performed in block 104 (Otto, ¶0053, Fig. 5), an "**initial radiation beam arrangement**" would be calculated based on the desired

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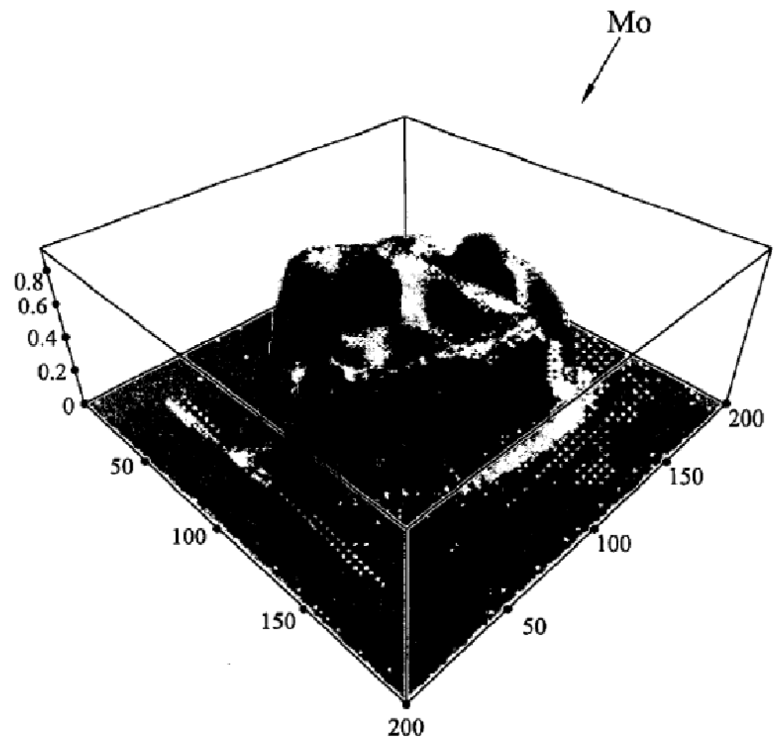
[3] The claimed "**desired prescription**" would also be satisfied by the physician-specified prescription from which the desired radiation field was originally derived (*e.g.*, by a treatment planning system). (Otto, ¶¶0039 ("The desired overall radiation field is derived by a treatment planning system in response to a <u>prescription specified by a physician</u>."), 0044.) Because the desired radiation field input into Otto's optimization process was originally derived from the physician-specified prescription, a beam arrangement calculated according to the desired radiation field would also have been calculated in accordance with the physician-specified prescription from which the input radiation field was derived. (Solberg, ¶68 n.2.)

radiation field and further optimized thereafter. (Solberg, ¶70.) This is confirmed by the evaluation step performed in block 106. (Otto, ¶0054, Fig. 5.) It would have been obvious that at least one radiation beam arrangement would be calculated so that "any discrepancies between the calculated spatial distribution of radiation resulting from the configurations determined in block 104 and the desired spatial distribution of radiation" could be evaluated. (Otto, ¶0054; Solberg, ¶70.)

Otto does not disclose the precise format of the desired radiation field ("**desired prescription**") input in block 102A, and Chang is thus cited for this implementation detail. Chang teaches that a desired radiation field can be specified using what it calls a "smooth" intensity map:

> In accordance with the method, a treatment dose optimization routine is performed to generate one or more continuous, smooth intensity maps representing the ideal treatment for a patient afflicted with a tumor. The number of intensity maps generated will depend on the number of treatment fields. An example of an ideal intensity map is shown in FIG. 4 and generally designated M0.

(Chang, 7:66-8:5.) This is shown below:




(Chang, Fig. 4.) Chang calls this a "continuous" or "smooth" map because it has a high resolution – one that is not limited by any particular treatment device – and thus provides a better representation of the ideal treatment. (Chang, 1:43-53, 8:6-15.)

**Rationale and Motivation to Combine:** It would have been obvious to combine Otto with Chang. (Solberg, ¶¶72-74.) The combination would have predictably resulted in Otto's method of determining the optimized parameters, including leaf positions and collimator angle, of a sequence of MLC configurations used to form a beam arrangement for applying radiation (Otto, ¶¶0044-56, Fig. 5), in which the desired prescription is provided in the form of a high resolution intensity map as disclosed in Chang. (Chang, 7:66-8:5, Fig. 4.)

Otto and Chang are analogous references in the field of intensity modulated radiation therapy. (Solberg, ¶72.) Both Otto and Chang, in fact, describe techniques for generating a sequence of MLC configurations for delivering radiation. (*E.g.*, Otto, ¶0011; Chang, 5:20-23.) A person of ordinary skill, looking to implement or enhance the MLC techniques of Otto, would have naturally consulted Chang for guidance in doing so. (Solberg, ¶72.) Chang provides an implementation detail missing from Otto – the format in which the desired radiation field can be provided.

Chang also provides express motivations to combine. Chang explains that its "smooth" intensity map has a higher spatial resolution than "discrete" maps used by alternative techniques, and therefore provides a superior representation of the desired treatment, which can ultimately enhance the quality of the actual treatment delivered:

> One difference in dose optimization algorithms is the resolution of the intensity map they generate, i.e., whether the intensity map is continuous or discrete. When the limitations of treatment delivery technique are taken into consideration in the dose optimization process, such as occurs in conventional multi-leaf collimator (MLC) treatment delivery techniques (described hereinbelow), the resulting intensity maps are discrete. <u>When these limitations are not considered, the optimization can often produce continuous intensity maps that represent the ideal IMRT treatment</u>. It has been demonstrated that the dosimetric quality of an actual IMRT treatment can be considerably affected by the resolution of the delivery technique compared to the ideal treatment.

(Chang, 1:43-57; *see also id*., 8:59-67.)

Using a high resolution intensity map also provides a better, "gold standard" against which computer-generated MLC configurations can be evaluated:

> [I]t is desirable for the dose optimization algorithm to design the intensity map without considering the treatment delivery device limitation. This way, ideal treatment using high-resolution intensity maps is generated and used for MLC segmentation. <u>The result of the ideal treatment can be used as the gold standard to evaluate the quality of a deliverable MLC treatment</u>.

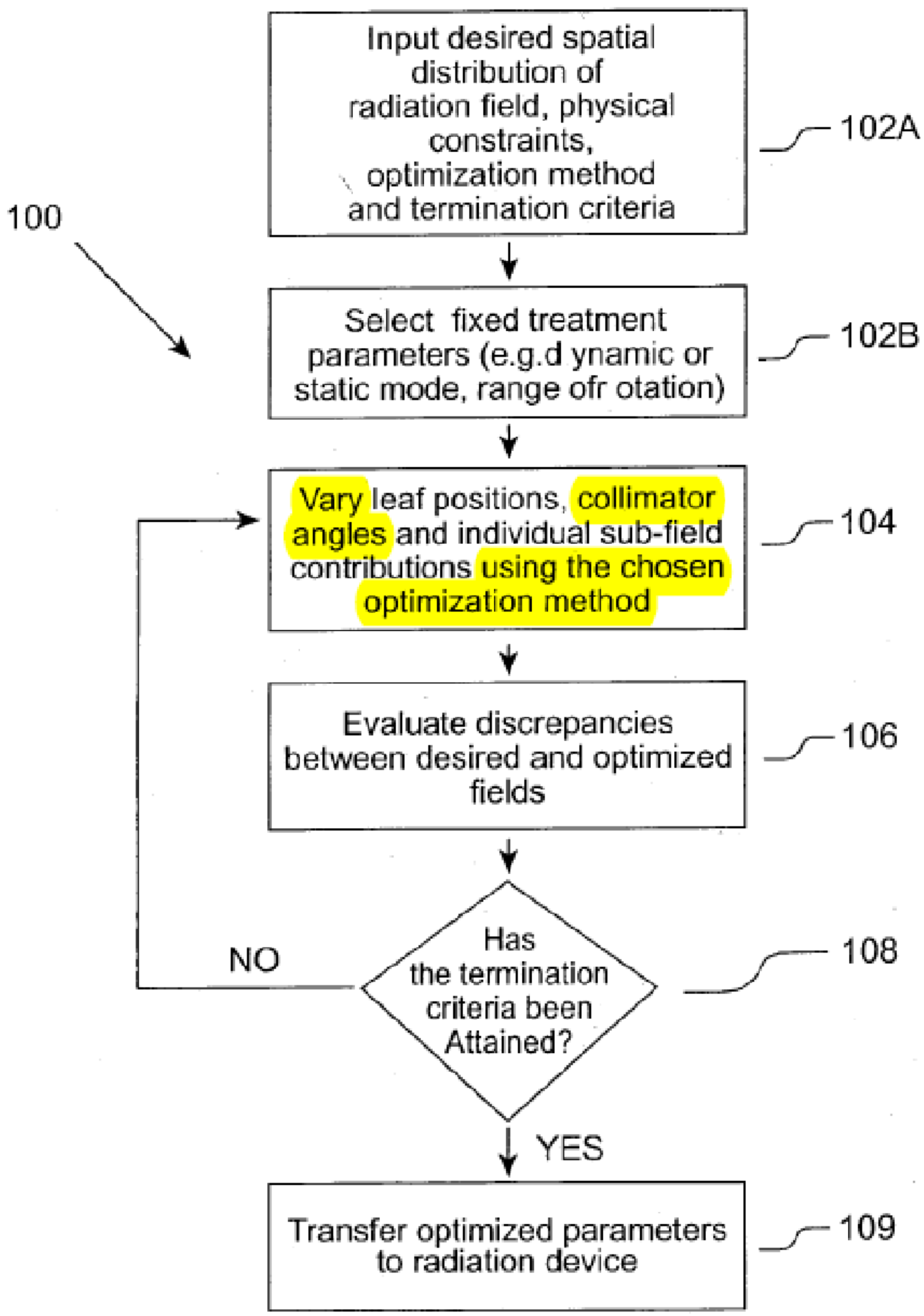
(Chang, 8:8-15.) This benefit would have been especially compelling in the context of Otto, which attempts to generate MLC configurations that are "optimized." (Otto, *e.g.*, ¶0056, Fig. 5; Solberg, ¶74.)

**(b) "changing the radiation beam arrangement by incorporating a first cost function to determine the collimator angle of the multi-leaf collimator, the first cost function including both a second cost function to enhance delivery efficiency by reducing a number of radiation beam segments and reducing a number of radiation beam monitor units required for delivery of the desired prescription and a third cost function to enhance conformity of the radiation beam arrangement to a target shape." (1[b])**

Due to its length, Petitioner addresses claim 1[b] in pieces to ensure clarity in application of the prior art to the claim language.

<u>"changing the radiation beam arrangement... to determine the collimator angle of the multi-leaf collimator"</u>: This limitation is disclosed and rendered obvious by

**Otto** in view of **Chang**. As mentioned, Otto generates MLC configurations for a desired radiation field by iteratively varying certain parameters, including collimator angle, according to a chosen optimization method. (Otto, ¶0053, Fig. 5; Solberg, ¶70.) This is shown in Figure 5:



(Otto, Fig. 5.) A person of ordinary skill would have understood and found it obvious that as part of the optimization step shown in block 104, the radiation beam arrangement would be "**chang[ed]**" by varying its parameters until an optimal collimator angle is determined. (Solberg, ¶76.)

Otto does not appear to teach any particular criteria for evaluating when an optimal collimator angle has been achieved, but this detail is again supplied by Chang. Chang teaches a specific technique in which the final optimal solution for collimator angle is chosen to fulfill the dual objectives of (1) "find[ing] the collimator angle that <u>conforms to the contour</u> as closely as possible" (Chang, 10:34-36, Fig. 8A, Fig. 8B), while (2) factoring in "the influence of such solution... on <u>treatment delivery efficiency</u>" (Chang, 11:10-12). (*See also* Chang, 10:32-11:12; Solberg, ¶¶77-80.) Chang further teaches that a single collimator angle can be chosen for all MLC configurations used to deliver the radiation field "to increase treatment delivery efficiency" (Chang, 11:7-9).

A person of ordinary skill would have been amply motivated to adapt these techniques from Chang to the MLC optimization process described in Otto, as will be explained in detail below. (Solberg, ¶¶80 n.4, 97, 103-106.) As Chang clearly demonstrates, the assertion of the '490 patent that in the prior art techniques "by which the conformity for targets is prioritized," "<u>no consideration is given to delivery efficiency</u>," is wholly inaccurate. ('490, 1:43-44; *compare with*, Chang, 10:34-36 ("The first solution finds the collimator angle that conforms to the contour as closely as possible, i.e., better definition of the intensity map."), 11:10-12 ("According to one aspect of the method, the final solution or solutions is chosen based [sic: on] the influence of such solution or solutions on ***treatment delivery efficiency***."), 11:7-9 ("An optimal collimator angle can also be selected for all segments of the same IM field to increase ***treatment delivery efficiency***.").)

"incorporating a first cost function" to determine the collimator angle, "the first cost function including both a second cost function to enhance delivery efficiency... and a third cost function to enhance conformity of the radiation beam arrangement to a target shape": As just explained, Chang expressly teaches choosing the collimator angle to further the two objectives recited in the claim language: (1) "**enhance conformity of the radiation beam arrangement to a target shape**"; and (2) "**enhance delivery efficiency**." Restated here, Chang teaches "find[ing] the collimator angle that conforms to the contour as closely as possible" (Chang, 10:34-36, Fig. 8A, Fig. 8B), while also factoring in "the influence of such solution... on treatment delivery efficiency" (Chang, 11:10-12).[4]

[4] The contour of Chang's ideal "smooth" intensity map represents the contour of the radiation target. (Chang, 9:34-44; Solberg, 81 n.5.) Conforming to the contour of Chang's smooth intensity map thus conforms to the shape of the radiation target.

Chang does not detail the precise computational technique that would be used to achieve its dual objectives of (1) "find[ing] the collimator angle that conforms to the contour as closely as possible" (Chang, 10:34-36, Fig. 8A, Fig. 8B), while (2) factoring in "the influence of such solution... on treatment delivery efficiency" (Chang, 11:10-12). But it would have been natural and obvious to use a "**cost function**" as claimed. (Solberg, ¶¶82, 32-33, 49.) In the context of radiation therapy, as discussed in the Technology Background provided above, a "**cost function**" is nothing more than a standard and age-old mathematical technique used to optimize the characteristics of treatment beams. As the Federal Circuit has recognized, "[a] patent need not teach, and preferably omits, what is well known in the art." *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987).

This is expressly confirmed in **Webb**, a foundational 1993 textbook entitled *The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning*, which provides the following definition for "**cost function**" in its "Glossary of Terms":

> **COST FUNCTION**: Mathematical function parametrizing the effect of arranging beams in some particular way. For example, a simple cost

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(*Compare* Chang, Fig. 11 (showing the MLC leaves conforming to contour of the intensity map), *with* 490, Figs. 10 & 11 (showing the MLC leaves conforming to contour of a cube and ellipsoid target, respectively).)

> 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, 344.)[5]

As Webb makes clear, a cost function allows the computer running an optimization process to identify when it has arrived at the optimal solution for a beam arrangement – the optimal solution corresponds to when the minimum value of the cost function has been reached. A person of ordinary skill would have thus understood, and been well aware, that the desired objective or objectives to be achieved through optimization would be specified through the mathematical function or functions used as the cost function of a given optimization process. (Webb, 344 ("**COST FUNCTION**: Mathematical function parametrizing the effect of arranging beams in some particular way.... The aim of optimization would be to

[5] The use of cost functions to optimize radiation beams was also admitted to be prior art as early as 1997 by U.S. Patent 6,038,283, which is another patent that has been asserted by Patent Owner in the underlying litigation. (Ex. 1012, 3:17-21 ("Existing methods and apparatus utilize a computational method of establishing optimized treatment plans based on an objective cost function that attributes costs of radiation of various portions of both the tumor and surrounding tissues, or structures.").)

minimize the cost function....”); Solberg, ¶83.)

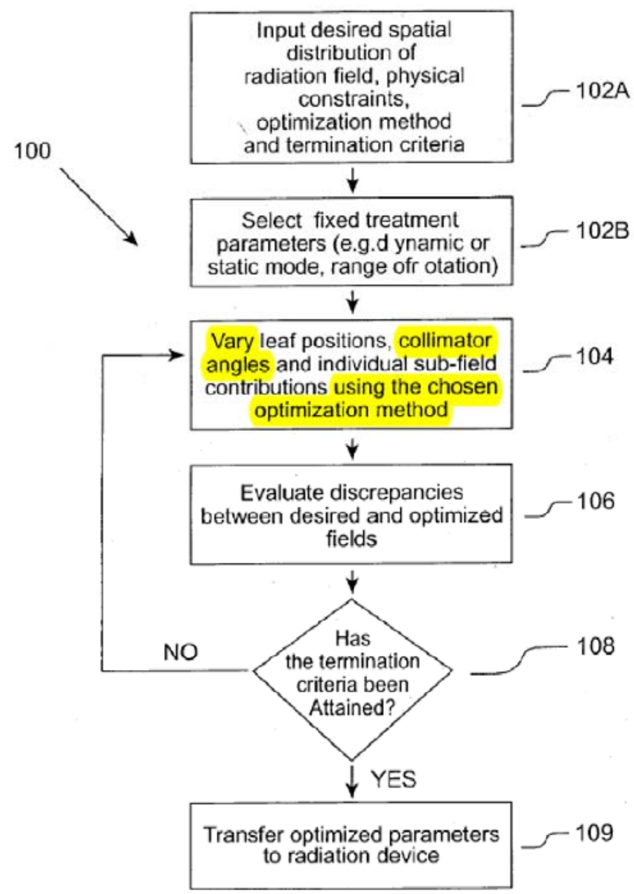
Webb also describes a foundational mathematical technique for determining a collimator angle that best achieves the specific objective of enhancing conformity to a radiation target, known as “Brahme’s Theory of Orientation.” (Webb, 233-235.) As Webb explains, “Brahme (1988) provided the arguments to answer the question of the optimal angulation of the MLC leaves (at some particular static orientation relative to the target volume).” (Webb, 233.) Under Brahme’s theory, the optimal collimator angle is identified by *minimizing the area seen* in the beam’s-eye-view of normal tissue outside the target volume:

> The problem reduces to finding the optimum way of arranging the leaves so as to <u>minimize the volume (represented by an area ‘seen’ in the beam’s-eye-view) of normal tissue outside the target volume</u>. This unwanted area arises because target regions do not have convenient stepped outlines and cannot be precisely matched by MLCs with leaves of finite width. Indeed, by considering a large number of possible ways of fitting an elliptical area with an MLC of leaf width 1 cm, Brahme (1988) showed that poor arrangements could lead to up to 20% more area being treated than necessary.

(Webb, 234.)

Webb thus teaches and suggests a “**cost function to enhance conformity of the radiation beam arrangement to a target shape**.” (Solberg, ¶85.) The ’490 patent also freely admits that this claimed technique was known – in fact, the “most common practice" – in the prior art. ('490, 1:33-42 ("When determining collimator angles in intensity modulated radiation therapy treatment . . . for use with a MLC radiation delivery system, <u>the most common practice currently is to select collimator rotation angles so that the MLC can be best conformed to the shape of the target, or lesion, in the radiation beam's eye view, or beams eye view ('BEV'). The algorithm used is based upon Brahme's orientation theory, by which the conformity for targets is prioritized</u>."), 2:7-11.)

Moreover, as discussed, Chang taught a technique in which the optimal solution for collimator angle to achieve conformity also accounted for treatment delivery efficiency. (Chang, 10:34-36 ("The first solution finds the collimator angle that conforms to the contour as closely as possible, i.e., better definition of the intensity map."), 11:10-12 ("According to one aspect of the method, the final solution or solutions is chosen based [sic; on] the influence of such solution or solutions on treatment delivery efficiency.").) It would therefore have been obvious that to



achieve Chang's dual objectives in the context of an iterative optimization process as disclosed in Otto (Otto, Fig. 5 (annotated above right)), a cost function would be used that included not just a mathematical function that quantified conformity (*e.g.*, Webb, 234), but also a function that quantified delivery efficiency.[6] And for this, a person of ordinary skill would have looked to **Mohan**.

As mentioned, Otto discloses a technique for "dynamic" MLC delivery, in which "the leaves are moved while the beam is on." (Otto, ¶0006.) **Mohan** teaches a known mathematical function for the minimum number of MUs, also referred to as "beam-on time," required to deliver a given radiation field from a particular direction of leaf travel. (Mohan, *e.g.*, 1227 (right column) ("Coordinates (*x*,*y*) are in the 'fanline' system, x being the direction parallel to leaf motion. Ω(*x*,*y*) is that

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[6] It is fundamental knowledge that cost functions operate by outputting a single value that quantifies the extent to which a proposed solution meets the desired objectives. (Webb, 344; Solberg ¶86 n.7.) To choose the "final solution" for conformity "based [on] the influence of such solution or solutions on treatment delivery efficiency" as taught by Chang, therefore, the value of the cost function would not depend solely on the degree of conformity achieved by a proposed solution for collimator angle, but also vary based on the degree of delivery efficiency associated with that solution. (Chang, 10:34-36, 11:10-12.)

portion of the total 'beam-on time' for which the point (*x, y, z*) is exposed to the source of the primary direct radiation unobstructed by dynamic leaves as the window formed by the leaves sweeps across the field. The term 'beam-on time' is used here not to describe the actual time but to describe the number of MUs for which the beam is on. We use the two terms interchangeably in this paper.") (brackets omitted), 1228 (right column) – 1229 (left column) ("*M* is the total beam-on time, which is not known *a priori*.... In order to <u>deliver the treatment as rapidly as possible</u>, at any one instant, one of the leaves of the pair <u>must travel at its maximum permissible velocity</u>.") (underlining added); Solberg, ¶87.)

As Mohan explains, "[t]he total beam-on time M is the maximum of the beam-on times of individual leaf pairs":

$$M = \max\{M_l\}. \qquad (10)$$

(Mohan, 1229 (left column).)

The beam-on time for a particular leaf pair, M l, 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).) Dr. Solberg has spelled out the meaning of the various terms that appear in equation 7 above:

- ${}^{X}i_{\text{start}}$ refers to the starting position of the leaf pair, which is the grid point just before the first nonzero element of the row in the radiation field corresponding to the path of leaf travel.
- ${}^{X}i_{\text{last}}$ refers to the terminal position of the leaf pair, which is the grid point just after the last nonzero element of the row in the radiation field corresponding to the path of leaf travel.
- $\Omega_e$ refers to the radiation intensity to be delivered at each discrete point in the path of leaf travel, the resolution of which is determined by the physical limitations of the delivery device. (Mohan, *e.g.*, 1228 (left column) ("The points along the direction of leaf motion (x direction) represent a row through the middle of each leaf.... [T]he grid size along the x-axis is as small as practical (1–4 mm).").)

(Solberg, ¶89.)

According to Dr. Solberg, the left term in equation (7) is proportional to the leaf travel distance for the leaf pair, ${}^{X}i_{\text{start}}$ — ${}^{X}i_{\text{last}}$. (Solberg, ¶90.) And the right term captures the amount of "complexity" or fluctuation in radiation intensity in the direction of leaf travel. (Mohan, 1229 (left column) ("The contribution of the first term to the beam-on time is the same regardless of the intensity fluctuations, but <u>the contribution of the second term depends upon the complexity of the opening density</u>

profile.”).)

Equation (7) from Mohan thus illustrates that, “if the opening density falls and then rises for some of the points, the beam-on time will increase depending upon both the frequency and the amplitude of the fluctuations.” (Mohan, 1229 (left column).) “As may be intuitively obvious... 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); Solberg, ¶85.)

Importantly, Mohan specifically teaches “optimiz[ing] the collimator angle for each beam in order to find orientations which minimize fluctuations.” (Mohan, 1237 (left column).) This teaching, along with Mohan’s explicit references to the precise mathematical function that would quantify the degree of fluctuation, would have motivated a person of ordinary skill to implement Mohan’s equations as part of a cost function. (Solberg, ¶¶91, 107.)

Dr. Solberg has also explained that equation (7) from Mohan is similar to the purportedly inventive equation for “effective leaf travel distance” disclosed in the ’490 patent (’490, 6:13-34), because Mohan’s equation accounts for both leaf travel distance and intensity fluctuations, which are often the result of transitions between tumor targets and neighboring organs at risk. (*Compare with*, ’490, 6:29-31 (“n is the number of separated target regions in the path of the MLC leaf pair, or leaf travel distance of an individual MLC leaf pair"), 6:31-32 ("$m_i$ is the leaf travel distance in the ith isolated target region for the MLC leaf pair"); *see also* Chang, 7:41-44 ("It has been found that the high gradient regions of the intensity map often divide the planned treatment volume (PTV) and the nearby organ at risk (OAR)."); Solberg, ¶92.)[7]

Under the combination of Otto and Chang with Webb and Mohan, therefore, the overall "**cost function**" used to achieve Chang's dual objectives in the context of Otto's optimization would include not only (1) a mathematical function that minimized the "area 'seen' in the beam's-eye-view" of normal tissue outside the target volume (Webb, 234), i.e., "**a [] cost function to enhance conformity of the radiation beam arrangement to a target shape**," but also (2) a function that minimized the number of MUs ("beam-on time") required to deliver a given radiation field from a particular orientation of leaf travel (Mohan, 1229 (equation 10, which incorporates equation 7), 1237 (left column)), i.e., "**a second cost function to enhance delivery efficiency by reducing a number of radiation beam segments and reducing a number of radiation beam monitor units required for delivery of the desired prescription**." (Solberg, ¶93.)

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[7] As noted in Mohan, equation (7) actually dates back to two papers by Spirou *et al*. from 1994 and 1996. (Mohan, 1229 (left column), 1237 (right column).)

Mohan does not expressly discuss the concept of "**radiation beam segments**" in relation to the equation that governs "beam-on time" as quantified in MUs. Nevertheless, a person of ordinary skill would have understood and found it obvious that Mohan's mathematical function for MUs, when used in a cost function, would result in solutions that "**reduc[e] a number of radiation beam segments**," as claimed. (Solberg, ¶94.) It is well-known that there exists a general correlation between the number of MUs and the number of segments – in Mohan's parlance, "windows formed by the leaves" (Mohan, 1226) – used to deliver a treatment plan. (Solberg, ¶94.)

This is further confirmed in Mohan itself. Figure 3 shows the MUs and corresponding leaf trajectories across the same travel distance for three different beam intensity patterns:

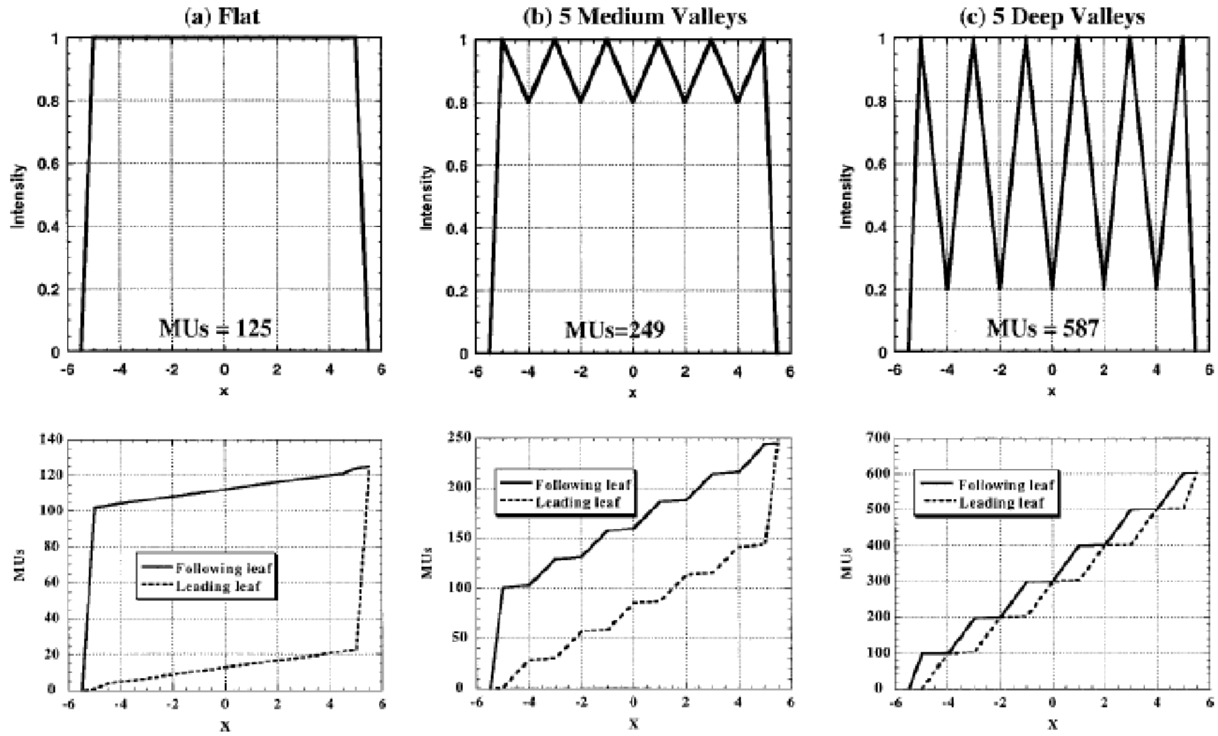



FIG. 3. Dependence of leaf trajectory and window width on the fluctuations of the intensity pattern.

(Mohan, 1232 (Fig. 3).) As shown above, as the number of MUs increased from left to right (pattern (a) to pattern (c)), the corresponding window widths not only decreased but exhibited greater variation – reflecting an increased number of MLC configurations implemented as the leaf pair travels from its starting to end points. (Solberg, ¶94.)

The general correlation is also confirmed by the ’490 patent. For example, dependent claim 5 specifies that the “**second cost function to enhance delivery efficiency by reducing a number of radiation beam segments and reducing a number of radiation beam monitor units**,” as originally recited in claim 1, can take the form of “max[le(θ)],” which outputs a single value “describing the maximum effective length." By expressly reciting a single value ("value of the maximum effective length") output by the "**second cost function**" that fulfills having "**reduc[ed] a number of radiation beam segments and reduc[ed] a number of radiation beam monitor units**" as required by claim 1, claim 5 confirms that the number of beam segments is directly correlated with the number of MUs. The '490 specification also discloses no separate mathematical function or algorithm for reducing beam segments as distinguished from reducing MUs. ('490, *e.g.*, 4:35-43 ("The function includes parameters to enhance delivery efficiency by reducing a number of segments and reducing a number of monitor units required for delivery of a desired radiation prescription. These parameters can include a value of a maximum effective length for a multi-leaf collimator pair leaf of the plurality of multi-leaf collimator pair leafs having the maximum effective length.").)

The correlation between beam segments and MUs is also confirmed in App. No. 60/487,067, which was filed in July 2003, before the earliest effective priority date of the '490 patent. (Ex. 1007.) App. No. 60/487,067 is a Provisional application to which U.S. Patent No. 7,266,175, which is another patent asserted by the Patent Owner in the underlying litigation. App. No. 60/487,067 states, consistent with the knowledge possessed by persons of ordinary skill:

> For multileaf collimation, or collimator, (MLC) treatment plans, radiation therapy treatment involves delivering radiation in a series of shaped segments, and treatment time and delivery efficiency are

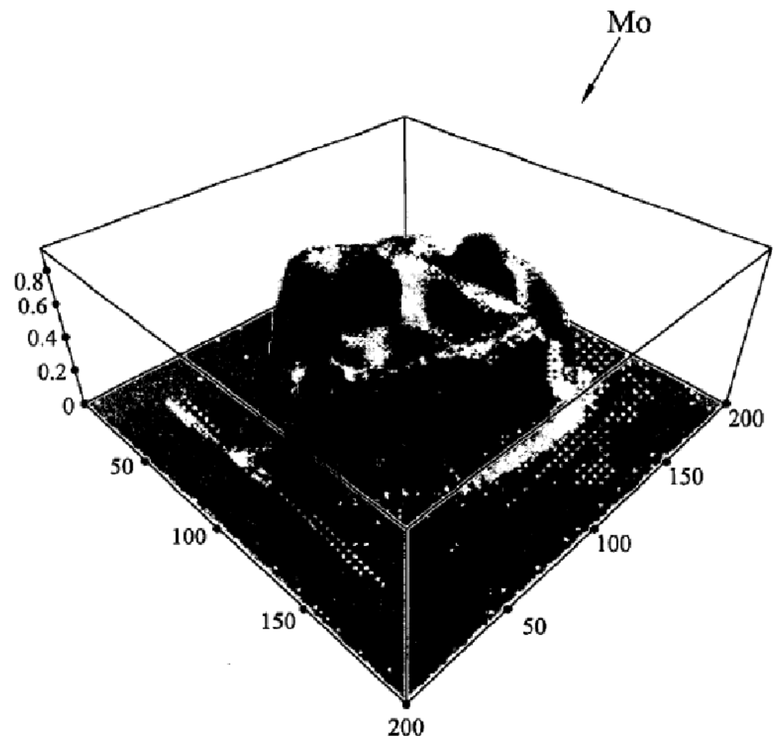
> proportional to the number of required segments, which is the Segment Count or Segmentation Count.

(Ex. 1007, ¶0004; Solberg, ¶96.) As discussed, the number of MUs calculated by the mathematical function in Mohan ("beam-on time") is proportional to the treatment time, and would thus also be proportional to the number of segments. (Solberg, ¶96.)

**Rationale and Motivation to Combine**: It would have been obvious to combine Otto, Chang, Webb, and Mohan. (Solberg, ¶¶97-108.) The combination would have predictably resulted in Otto's method of determining the optimized parameters, including collimator angle, of a sequence of MLC configurations used to form a beam arrangement (Otto, ¶¶0044-56, Fig. 5), in which the optimized collimator angle is determined by incorporating a cost function, as disclosed by the combined teachings of Chang, Webb, and Mohan. (*E.g.*, Chang, 10:34-36, 11:10¬12; Webb, 234, 234; Mohan, 1229; Solberg, ¶91.) This cost function, as explained above, implements Chang's dual objectives to "find[] the collimator angle that conforms to the contour as closely as possible," while also factoring in "the influence of such solution... on treatment delivery efficiency." (Chang, 10:34-35, 11:10-12.) The cost function accordingly includes (1) a mathematical function that minimizes the "area 'seen' in the beam's-eye-view" of normal tissue outside the target volume (Webb, 234 (Brahme)), to enhance conformity of the beam arrangement to a target shape; and (2) a mathematical function that minimizes the number of MUs ("beam-on time") required to deliver a desired radiation field (Mohan, 1229 (left column) (equation 10, which incorporates equation 7), 1237 (left column)), to enhance delivery efficiency by reducing a number of beam segments and MUs. (Solberg, ¶97.)

It is well-settled that obviousness does not require a showing of a physical combination of the references, or show how the elements of the secondary references could be bodily incorporated into the system disclosed in a primary reference. *See, e.g.*, *In re Etter*, 756 F.2d 852, 859 (Fed. Cir. 1985) (en banc); *see also In re Keller*, 642 F.2d 413, 425 (C.C.P.A. 1981). Nevertheless, for ease of understanding and to ensure clarity in how the prior art is being applied to the claim, Dr. Solberg has described at length one exemplary implementation of how the proposed combination of Otto, Chang, Webb, and Mohan would work in practice. (Solberg, ¶¶99-102.)

As Dr. Solberg explains, Otto would generate MLC configurations for a desired radiation field for "dynamic" delivery by iteratively varying certain parameters, including collimator angle. (Otto, ¶¶0006, 0053, Fig. 5; Solberg, ¶99.) And the desired radiation field would be input into Otto in the form of a high resolution, "smooth" intensity map as taught by Chang. (Chang, *e.g.*, 7:66-8:5, Fig. 4.) This is shown below:




(Chang, Fig. 4.)

For each collimator angle evaluated as part of Otto's optimization process (Otto, ¶0053, Fig. 5), the corresponding value of the overall cost function described above would be calculated. (Solberg, ¶100.) This would involve calculating the mathematical function for the area seen in the "beam's-eye-view" of normal tissue outside the target volume. (Webb, 234 (Brahme).) And this would be combined with the value for minimum MUs required to deliver the desired radiation in the orientation of leaf travel (corresponding to the collimator angle being evaluated), to yield a single value for the cost function. (Mohan, 1229 (left column) (equation 10, which incorporates equation 7), 1237 (left column); Solberg, ¶100.)

The optimal collimator angle is achieved when the value of the overall cost function is at a minimum, i.e., when the combination of the two outputs just described has reached its lowest value. (Webb, 344; Solberg, ¶101.) For a given desired radiation field as represented using Chang's "smooth" intensity map, this is the collimator angle that draws the appropriate balance between allowing the collimator leaves to conform as closely as possible to the contour of the target (as represented by the contour of the "smooth" intensity map) (Webb, 234; Chang, Fig. 8B), and allowing the collimator leaves to travel in a direction with a short leaf travel distance and minimized fluctuations in intensity, and thereby deliver the desired radiation with improved efficiency. (Mohan, 1229 (left column), 1231 (left column), ), 1237 (left column) ("[O]ptimize the collimator angle for each beam in order to find orientations which minimize fluctuations.").)

As mentioned, Chang teaches that "[a]n optimal collimator angle can also be selected for all segments of the same IM field to increase treatment delivery efficiency." (Chang, 11:7-12.) A single optimized collimator angle could accordingly be used for the entire sequence of MLC configurations to deliver the desired field (i.e., from a particular gantry angle) to further enhance delivery efficiency. (Solberg, ¶102.)

Otto, Chang, Webb, and Mohan are all analogous references in the field of intensity modulated radiation therapy. (Solberg, ¶103.) A person of ordinary skill, looking to implement or enhance the MLC optimization techniques of Otto, would have naturally consulted Chang, Webb, and Mohan for guidance in doing so. (*Id*.) And a person of ordinary skill would have had every expectation that their combination would be successful. (Solberg, *e.g.*, ¶100 n.9.) Indeed, each of these references cite to other works by many of the same authors. (*Id*.) The close collaboration exhibited in the field of radiotherapy, and the closely analogous nature of the references, would themselves have provided suggestions to combine. (*Id*.)

A person of ordinary skill would also have been motivated to combine in the manner described above because of the many distinct advantages that would be provided. (Solberg, ¶104.) As explained, a cost function would have been a natural (if not essential) component of the iterative optimization process described in Otto. (Otto, Fig. 5.) By distilling the suitability of potential solutions down to a single value, it allows the optimization system to progress through a vast number of candidates to identify the best possible solution. (Solberg, ¶104.) The precise formulation of the cost function would also have provided the user with direct control over the desired degree of conformity as balanced against its potential influence on delivery efficiency in the final solution. (Chang, 10:34-36, 11:10-12; Solberg, ¶104.).) As noted, cost functions had been a staple technique in the context of beam optimization for decades prior to the alleged invention. (Webb, 344.)

Moreover, Chang provides express motivations to specifically optimize the collimator angle of the MLC. Chang explains that doing so can minimize the jaggedness of the contour of the radiation field, i.e., enhance conformity, and also reduce the discrepancy between the desired radiation field and the radiation actually delivered (which Chang calls the "discrete 'skyscraper' map"):

> The angle of the collimator can have a significant influence of the discrepancy between the discrete "skyscraper" IM map and its corresponding original smooth map. The effect of the collimator angle is similar to that in conforming an MLC opening to a given treatment portal defined by a conventional block. An optimal collimator angle can minimize the jaggedness of the edge or contour of the field defined by the MLC opening. An optimal collimator angle can reduce the difference between the discrete IM map and its original smooth map. Therefore, it is proposed herein that the orientation of the MLC leaves or collimator angle should be considered as a variable in the MLC-IM treatment delivery optimization process.

(Chang, 3:66-4:12.)

More generally, optimizing the collimator angle can improve the quality and efficiency of the treatment:

> For discrete MLC-IMRT techniques, the orientation of the MLC leaves can have a considerable influence on the quality and efficiency of the treatment. The present method also recognizes that MLC leaves can be translated to any position within their operating range to a great degree of accuracy (i.e., micro-scale). As indicated hereinabove, previous methods have not taken advantage of the continuous positioning capability of the MLC hardware of commercially available medical

> LINAC systems, but rather position MLC leaves by indexing them in 1-cm increments. The present method, on the other hand, takes full advantage of both the continuous MLC leaf positioning and the continuous collimator angle selection available in MLC-equipped radiotherapy machines. Optimization of collimator orientation assists in generating a more accurate intensity map with less required segment fields.

(Chang, 9:52-67.) A person of ordinary skill would have appreciated that these benefits apply to the "dynamic" MLC technique described in Otto (Otto, *e.g.*, ¶0006), and would thus have been motivated to adapt Chang's teachings to Otto's optimization process. (Solberg, ¶106.)

Webb and Mohan similarly teach the benefits of an optimized collimator angle. Webb explains that selecting a collimator angle to enhance conformity to the target reduces the overdose of radiation to an "unwanted area" outside the target that occurs "because target regions do not have convenient stepped outlines and cannot be precisely matched by MLCs with leaves of finite width." (Webb, 234.) Mohan, for its part, teaches optimizing the collimator angle for a beam "in order to find orientations which minimize fluctuations" or complexity in beam intensity. (Mohan, 1237 (left column).) This is because <u>"[m]ore complex intensity patterns take longer (i.e., require more MUs) to deliver</u> and, due to the contribution received from leaf transmission and scatter, impose a high lower limit on the minimum intensity received by a point, and may, therefore, negatively affect the quality and accuracy of dose distributions." (Mohan, 1226 (left column).)

Petitioner has thus explained at length the specific motivations – many of which expressly taught – that would have led a person of ordinary skill to arrive at the claimed invention based on the combined teachings of Otto, Chang, Webb, and Mohan. To the extent the Patent Owner attempts to seize upon other alternatives presented by the prior art to show a lack of motivation to combine, Federal Circuit law is clear that "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed." *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). (*See also* Solberg, ¶¶108, 80 n.4.)

**2. Claim 4: "A method as defined in claim 1, further comprising the step of: rejecting the change in the radiation beam arrangement if the change of the radiation beam arrangement significantly leads to a lesser correspondence to the desired prescription and accepting the change of the radiation beam arrangement if the change of the radiation beam arrangement both leads to more radiation delivery efficiency and does not lead to significantly less correspondence to the desired prescription."**

This additional limitation has been largely addressed in the discussion of claim 1[b] above. Under Petitioner's combination, as explained for claim 1, the overall cost function would include a mathematical function that outputs lower values when the evaluated collimator angle leads to greater conformity to the target shape, and thus the desired prescription. (*E.g.*, Chang, 10:34-36; Webb, 234.) The overall cost function would also include a mathematical function that outputs lower values when the evaluated collimator angle leads to enhanced delivery efficiency. (*E.g.*, Chang, 11:10-12; Mohan, 1229 (left column); Solberg, ¶¶110, 101.)

As was well-known to persons of ordinary skill, and explained in Webb's definition of "cost function," "[t]he aim of optimization would be to minimize the cost function...." (Webb, 344.) A person of ordinary skill would thus have understood and found it obvious that a change in the collimator angle (and thus a change in the beam arrangement) would be accepted only if the change led to a lower value for the overall cost function. (Solberg, ¶111.) And this would not occur if the change led to a significantly lesser correspondence to desired prescription, because this would significantly increase the value output by the mathematical function for enhancing conformity. (*Id.*)

If, on the other hand, the change does not lead to a significantly lesser correspondence to the desired prescription, the value output by the mathematical function for enhancing conformity would not increase by much, if at all. (Solberg, ¶112.) As a result, the value for the overall cost function would be lower if the change led to greater delivery efficiency, as the output of the mathematical function for enhancing delivery efficiency would now be lower. (*Id.*)

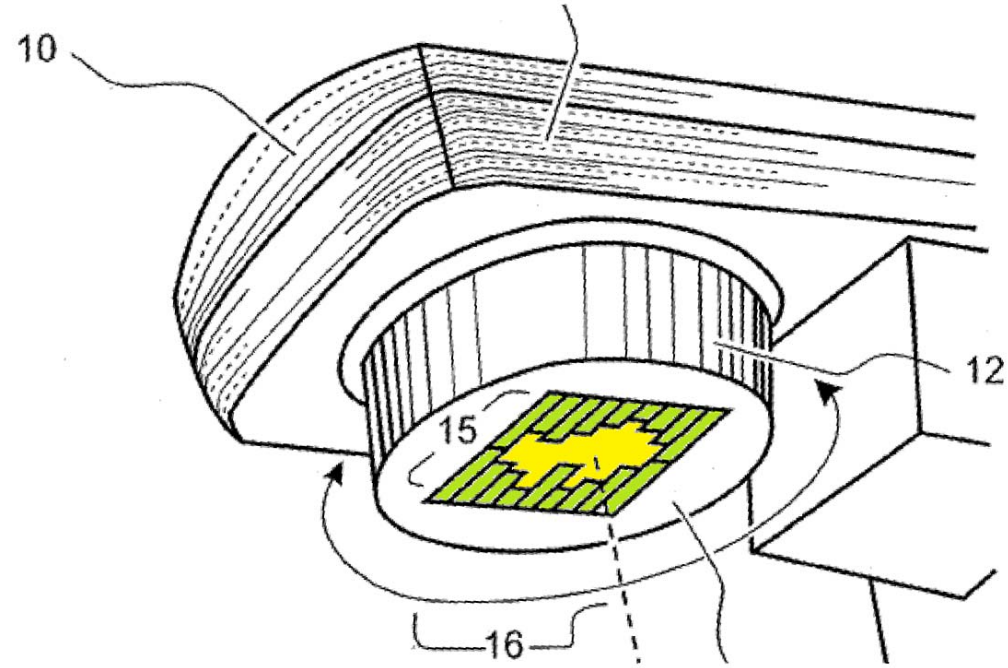
### 3. Claim 17

#### (a) "An apparatus for use in conformal radiation therapy of a target tumor, the apparatus comprising:" (17[preamble])

To the extent the preamble is limiting, it is disclosed by **Otto**. (Otto, *e.g.*, Fig. 1.)

#### (b) "a multi-leaf collimator having a plurality of selectable discrete collimator angles, an opening to pass a radiation beam, and a plurality of multi-leaf collimator leaf pairs to close portions of the opening to form a radiation beam arrangement having a plurality of radiation beam segments; and" (17[a])

As explained for the preamble of claim 1, Otto discloses and renders obvious "a multi-leaf collimator having... an opening to pass a radiation beam and a plurality of multi-leaf collimator leaf pairs to close portions of the opening to form a radiation beam arrangement having a plurality of radiation beam segments." This is depicted in Fig. 1 and described in the accompanying paragraphs of Otto.




(Otto, Fig. 1 (partial figure).)

As further explained for the preamble of claim 1, Otto discloses that the collimator angle can be varied to provide different field shapes for the radiation. This is shown in Figures 2A and 2B, which depict two exemplary MLC configurations that have different collimator angles (Otto, ¶¶0018, 0028):

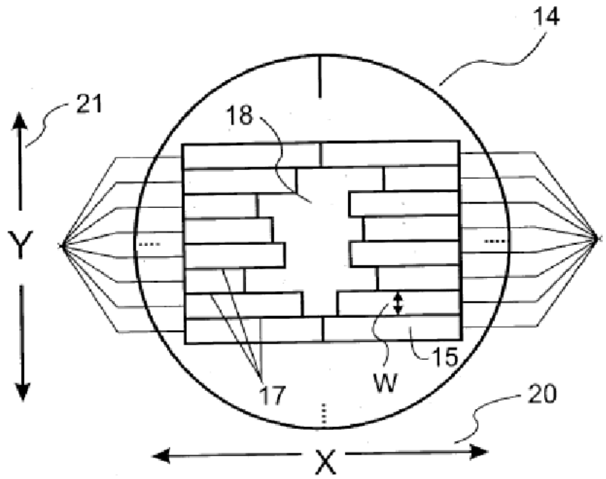



FIGURE 2A

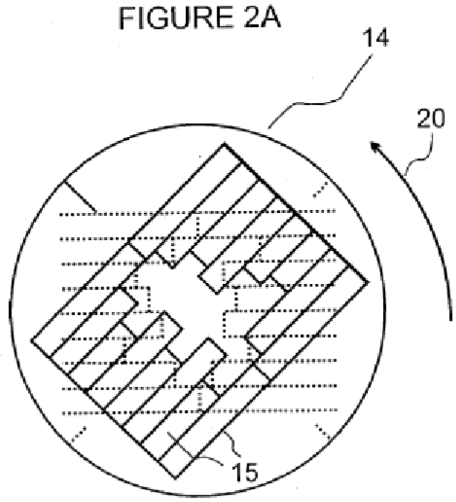



FIGURE 2B

(Otto, Figs. 2A, 2B.) Otto thus also teaches "a multi-leaf collimator having a plurality of selectable discrete collimator angles" as recited in claim 17.

**(c) "a computer in communication with the multi-leaf collimator to form the radiation beam arrangement incorporating a cost function to determine a collimator angle of the multi-leaf collimator to thereby enhance the radiation beam arrangement, the cost function including both parameters to enhance conformity of the radiation beam arrangement to a shape of the target, and parameters to enhance delivery efficiency by reducing a number of segments and reducing a number of monitor units required for delivery of a desired radiation prescription." (17[b])**

Claim 17[b] has largely been covered by the analysis provided for claim 1[b] above. Petitioner addresses a few differences in the claim language below.

Claim 17[b] recites "**a computer in communication with the multi-leaf collimator**." This is met by Otto's teaching that "[t]he control system [in FIG. 1] typically comprises a computer processor which receives parameters specifying the leaf positions and rotation angle for a sub field and actuates the mechanism to cause the leaves to move to the desired positions and to cause the multi-leaf collimator to be rotated to the desired angle." (Otto, ¶0026.)

Claim 17[b] also recites that the cost function includes "both ***parameters*** to enhance conformity of the radiation beam arrangement to a shape of the target and ***parameters*** to enhance delivery efficiency by reducing a number of segments and reducing a number of monitor units required for delivery of a desired radiation prescription." Although this uses slightly different language from the second "cost function" and third "cost function" included in the overall cost function of claim

1[b], the mapping provided for claim 1[b] applies equally here. It is fundamental knowledge to persons of ordinary skill that mathematical functions can be expressed using parameters. (See, *e.g.*, Ex. 1013, *Webster's Third New International Dictionary, Unabridged* (2002), 1638 (providing a definition for "parameter" as "an independent variable through functions of which other functions may be expressed"); Solberg, ¶119.) It would therefore have been obvious that each of the "second cost function" and "third cost function" mapped previously to claim 1[b] would be expressed using "**parameters**," as recited in claim 17[b]. (Solberg, ¶119.)

**4. Claim 18: "An apparatus as defined in claim 17, wherein the parameters to enhance delivery efficiency include a value of a maximum effective length for a multi-leaf collimator leaf pair of the plurality of multi-leaf collimator leaf pairs having the maximum effective length."**

The additional limitation in claim 18 has largely been covered by the analysis previously provided for claim 1[b]. As explained, **Mohan** teaches a mathematical function for determining the minimum number of MUs (also referred to as "beam-on time") required to deliver a given radiation field from a particular direction of leaf travel. (Mohan, *e.g.*, 1227 (right column), 1228 (right column) – 1229 (left column).)

The value of $M^l$, the beam-on time for a particular leaf pair in an MLC having multiple leaf pairs is given by:

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

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

- $x_{i_{\text{start}}}$ refers to the starting position of the leaf pair, which is the grid point just before the first nonzero element of the row in the radiation field corresponding to the path of leaf travel.
- $x_{i_{\text{last}}}$ refers to the terminal position of the leaf pair, which is the grid point just after the last nonzero element of the row in the radiation field corresponding to the path of leaf travel.
- $\Omega_e$ refers to the radiation intensity to be delivered at each discrete point in the path of leaf travel, the resolution of which is determined by the physical limitations of the delivery device.

(Solberg, ¶122.)

As explained by Dr. Solberg, the left term in equation (7) is proportional to the leaf travel distance for the leaf pair, $x_{i_{\text{start}}}$ — $x_{i_{\text{last}}}$. The right term captures the amount of "complexity" or fluctuation in radiation intensity in the direction of leaf travel. (Mohan, *e.g.*, 1229 (left column) ("The contribution of the first term to the beam-on time is the same regardless of the intensity fluctuations, but the contribution of the second term depends upon the complexity of the opening density profile."); Solberg ¶123.) $M^l$ is thus a value of "**effective length**," as claimed.

As explained for claim 1[b], the equation for $M^l$ is similar to the equation for "effective leaf travel distance" disclosed in the '490 patent ('490, 6:13-34), because equation for $M^l$ accounts for both leaf travel distance and intensity fluctuations, which are often the result of transitions between tumor targets and neighboring organs at risk. (*Compare with*, '490, 6:29-31 ("n is the number of separated target regions in the path of the MLC leaf pair, or leaf travel distance of an individual MLC leaf pair"), 6:31-32 ("mi is the leaf travel distance in the ith isolated target region for the MLC leaf pair"); *see also* Chang, 7:41-44 ("It has been found that the high gradient regions of the intensity map often divide the planned treatment volume (PTV) and the nearby organ at risk (OAR).").)

As further explained, Mohan teaches that "[t]he total beam-on time M is the maximum of the beam-on times of individual leaf pairs":

$$M = \max\{M_l\}. \qquad (10)$$

(Mohan, 1229 (left column).)

*M* is thus a value of the "***maximum*** **effective length**" for the MLC leaf pair in an MLC (which has multiple leaf pairs) that "**ha[s] the maximum effective length**," $M^l$ (Solberg ¶124.) As explained for claim 1[b], the equation for M would be adapted as the mathematical function for enhancing delivery efficiency in the overall cost function of the proposed combination.

#### 5. Claim 19: "An apparatus as defined in claim 18, wherein the parameters to enhance conformity of the radiation beam arrangement include an area difference between an area of an opening in the multi-leaf collimator which the multi-leaf collimator can define when approaching correspondence with a target shape in a beams eye view of the multi-leaf collimator, and an area of the target shape in the same beams eye view of the multi-leaf collimator, a view from the perspective of the opening in the multi-leaf collimator along an axis of the radiation beam defining the beams eye view of the multi-leaf collimator."

Claim 19 does no more than recite Brahme's orientation theory of the prior art, as admitted by the '490 patent:

> When determining collimator angles in intensity modulated radiation therapy treatment, or intensity modulated radiotherapy, ("IMRT") inverse treatment plans for use with a MLC radiation delivery system, the most common practice currently is to select collimator rotation angles so that the MLC can be best conformed to the shape of the target, or lesion, in the radiation beam's eye view, or beams eye view ("BEV"). The algorithm used is based upon Brahme's orientation theory, by which the conformity for targets is prioritized.... Note, the beams eye view is a view from the perspective of the opening in the multi-leaf collimator along an axis of the radiation beam.

('490, 1:33-46.)

In addition to being admitted prior art, Brahme's orientation theory is also expressly described in Webb:

> The problem reduces to finding the optimum way of arranging the leaves so as to minimize the volume (represented by an area 'seen' in the beam's-eye-view) of normal tissue outside the target volume. This unwanted area arises because target regions do not have convenient stepped outlines and cannot be precisely matched by MLCs with leaves of finite width. Indeed, by considering a large number of possible ways of fitting an elliptical area with an MLC of leaf width 1 cm, Brahme (1988) showed that poor arrangements could lead to up to 20% more area being treated than necessary.

(Webb, 234.) As explained for claim 1[b], the equation for Brahme's theory would be adapted as the mathematical function for enhancing conformity in the overall cost function of the proposed combination.

#### 6. Alternative Mapping for "Beam Segments" for All Claims

Each of claims 1, 14, and 17-19 addressed above recite "a radiation beam arrangement having a plurality of radiation beam segments," and "enhanc[ing] delivery efficiency by reducing a number of segments." As explained by Dr. Solberg, the term "**segments**" in the context of MLCs typically refers to the MLC configurations of a beam formed in sequence to deliver the desired radiation field. (Solberg, ¶129 (citing Chang, 2:45-51).) And in Petitioner's application of the prior art to the claims above, Petitioner mapped the claimed "**plurality of radiation beam segments**" consistent with typical usage to a sequence of MLC configurations used to deliver a radiation field from a particular gantry angle. (Otto, *e.g.*, ¶¶0005-0006, 0027.) Petitioner also explained how the mathematical function provided in Mohan, when used in the cost function of Petitioner's combination, would "**enhance delivery efficiency by reducing a number of segments**" by minimizing MUs – to which the number of MLC segments is generally correlated. (Mohan, *e.g.*, 1229.)

It is well-settled that claim terms are normally not interpreted in a way that excludes embodiments disclosed in the specification. *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276 (Fed. Cir. 2008). Based on the '490 specification, as explained below, the term "**segment**" or "**beam segment**" as recited in the patent claims would appear to encompass an additional interpretation slightly different from its typical usage discussed above. (Solberg, ¶¶130-132.)

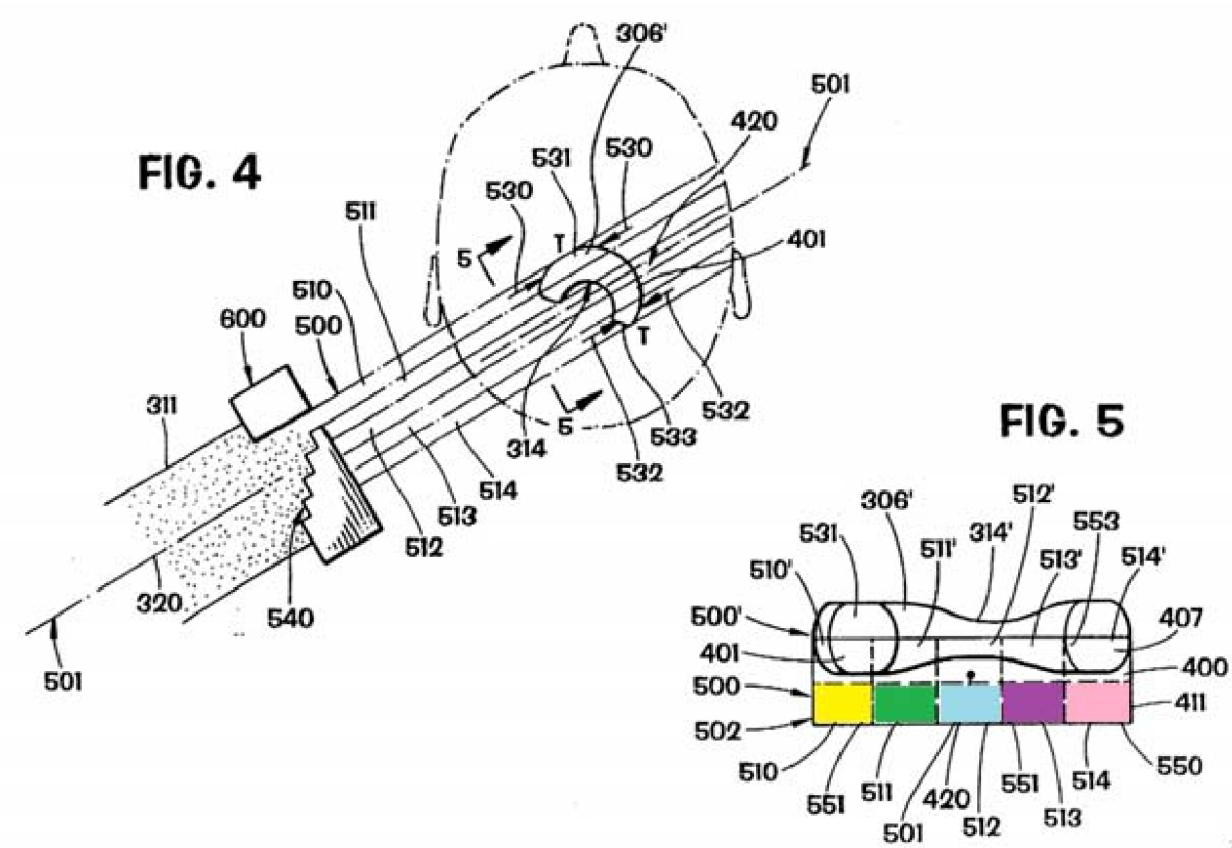
The '490 specification "incorporates by reference U.S. Pat. No. 5,596,619... and U.S. Pat. No. 5,802,136..." (the "incorporated patents"). (Exs. 1009-1010.) The incorporated patents both describe an embodiment of a radiation treatment beam 500 as follows:

> Preferably, the rectangular cross-sectional configuration 502 of the at least one radiation treatment beam 500 is separated into a plurality of radiation beam segments 510-514, in a manner which will be hereinafter described. The beam intensity of the plurality of radiation beam segments 510-514 of the radiation treatment beam 500 are then independently modulated across the rectangular cross-sectional configuration 502 of the radiation treatment beam 500.... Each radiation beam segment 510-514 of radiation treatment beam 500 may have a

beam intensity in accordance with the thickness of the part 401 of tumor 306' through which each radiation beam segment 510-514 passes.

(Ex. 1009, '619, 11:48-63; Ex. 1010, '136, 13:65-14:14 (same).)

This embodiment of radiation treatment beam 500 is shown in Figures 4 and 5 below:




(Ex. 1009, '619, Figs. 4, 5.)

A person of ordinary skill would have understood that "radiation beam segments 510-514," as indicated in color annotation above, show what are typically referred to as "beam elements" or "beamlets," which are small intensity modulated portions of a large beam, and thus distinct from MLC "segments." (Solberg, ¶132.)

This is consistent with the way "segments" are used in a declaration submitted during the prosecution of the U.S. Patent No. 7,266,175 by of Mark P. Carol, who is the named inventor of the incorporated patents.[8] That declaration states:

> IMRT is inherently an inefficient process. It uses a large number of beam segments (small portions or pieces of a large beam) each controlled individually and each delivered for a certain amount of time... The most efficient way to deliver radiation would be to use 100% of a small number of large beams. In IMRT one uses somewhat less than 100% of each of a large number of small beams (segments) in order to get a more conformal plan that spares more non-target tissue.

(Ex. 1014, Carol Declaration, 3, ¶6a1.)

As mentioned, claim terms are normally not interpreted in a way that excludes embodiments disclosed in the specification. *Oatey*, 514 F.3d at 1276. Thus, to the extent the "**segments**" of the '490 patent claims can be interpreted to encompass "beamlets" or "small portions of a large beam" in addition to its typical meaning, this would provide an alternative avenue through which the claimed "**segments**" can be met by Petitioner's combination.

This is because, as explained for claim 1[b], Mohan's equation as used in a cost function would drive solutions for an optimized collimator angle towards

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[8] U.S. Patent No. 7,266,175 has also been asserted by the Patent Owner against Petitioner in the underlying litigation.

orientations with *minimized fluctuations in intensity level*. (Mohan, *e.g.*, 1229 (left column) (equation 10, which incorporates equation 7), 1231 (left column) ("As may be intuitively obvious... 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."), 1237 (left column) ("[O]ptimize the collimator angle for each beam in order to find orientations which minimize fluctuations.") (underlining added).) And as the written description of the '490 patent makes clear, "the number of segments are considered reduced when adjacent segments have substantially the same intensity level." ('490, 1:47-49.)

Accordingly, to the extent "**segments**" encompasses "beamlets" or "small portions of a large beam," Mohan's equation as used in a cost function would meet the limitation of "**enhanc[ing] delivery efficiency by reducing a number of segments**" for the additional reason that it would drive the optimized collimator angle towards orientations with minimized fluctuations in intensity – that is, orientations where more "adjacent segments have substantially the same intensity level." ('490, 1:47-49.)

## IX. CONCLUSION

For the reasons set forth above, Elekta requests institution of review on the challenged claims.

Dated: May 21, 2020

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## CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. §42.24(d), the undersigned certifies that the foregoing Petition for *Inter Partes* Review of U.S. Patent No. 7,015,490 contains, as measured by the word-processing system used to prepare this paper, 11,821 words. This word count does not include the items excluded by 37 C.F.R. §42.24 as not counting towards the word limit.

Dated: May 21, 2020

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## CERTIFICATE OF SERVICE

The undersigned certifies pursuant to 37 C.F.R. §42.6(e) and §42.105 that on May 21, 2020, a true and correct copy of the foregoing **PETITION FOR INTER PARTES REVIEW**, including all supporting **EXHIBITS**, and Petitioner's **POWER OF ATTORNEY** are being served on the Patent Owner and counsel of record for the Patent Owner, via electronic mail and via Federal Express Overnight at the correspondence address of record as listed on PAIR:

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