UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

VARIAN MEDICAL SYSTEMS, INC.,
Petitioner

v.

BEST MEDICAL INTERNATIONAL, INC.
Patent Owner

Case No. IPR2020-00071

U.S. Patent No. 6,393,096 B1

Filing Date: May 27, 1999
Issue Date: May 21, 2002

Title: PLANNING METHOD AND APPARATUS FOR RADIATION DOSIMETRY

PETITION FOR *INTER PARTES* REVIEW
OF U.S. PATENT NO. 6,393,096 B1

TABLE OF CONTENTS

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF CONTENTS
(continued)

Page

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES
(continued)

Page(s)

Statutes

Other Authorities

EXHIBIT LIST

Exhibit No.	Description of Document
1001	U.S. Patent No. 6,393,096 B1 to Mark P. Carol et al. (filed May 27, 1999, issued May 21, 2002) ("'096 patent" or "'096")
1002	Declaration of Kenneth Gall
1003	Declaration of Sylvia Hall-Ellis, Ph.D.
1004	Declaration of Christopher Butler
1005	Notice of Allowance for US Application 09/320,980 dated Sept. 1, 2000
1006-1007	*Reserved*
1008	*The Physics of Three-Dimensional Radiation Therapy: Conformal Radiotherapy, Radiosurgery and Treatment Planning* (1993) ("Webb-1993")
1009	Webb, S., "Optimisation of conformal radiotherapy dose distribution by simulated annealing," *Phys. Med. Biol.*, 34(10):1349-1370 (1989) ("Webb-1989")
1010	Lawrence T.S. et al., "An Application of Dose Volume Histograms to the Treatment of Intrahepatic Malignancies with Radiation Therapy," *Int. J. Radiation Oncology Biol. Phys.*, 19:1041-1047 (1990) ("Lawrence-1990")
1011	Langer, M. et al., "Large Scale Optimization of Beam Weights Under Dose-Volume Restrictions," *Int. J. Radiation Oncology Biol. Phys.*, 18:887-893 (1990) ("Langer-1990")
1012	Goitein, M., "The Comparison of Treatment Plans," *Seminars in Radiation Oncology*, 2(4):246-256 (1992) ("Goitein-1992")

TABLE OF AUTHORITIES
(continued)

Page(s)

Exhibit No.	Description of Document
1013	Morrill, S.M., "Constrained simulated annealing for optimized radiation therapy treatment planning," *Computer Methods and Programs in Biomedicine*, 33:135-144 (1990) ("Morrill-1990")
1014	Webb, S., "Optimizing Radiation Therapy Inverse Treatment Planning Using the Simulated Annealing Technique," *International Journal of Imaging Sytems and Technology*, 6:71-79 (1995) ("Webb-1995")
1015	Viggars D.A., et al., "The Objective Evaluation of Alternative Treatment Plans III: The Quantitative Analysis of Dose Volume Histograms," *Int. J. Radiation Oncology Biol. Phys.*, 23:419-427 (1992) ("Viggars")
1016	Drzymala, R.E. et al., "Dose-Volume Histograms," *Int. J. Radiation Oncology Biol. Phys.*, 21:71-78 (1991) ("Drzymala-1991")
1017	U.S. Patent No. 5,596,619 ("'619 patent")
1018	Kirkpatrick, S. et al., "Optimization by Simulated Annealing," *Science* 220(4598):671-680 (1983) ("Kirkpatrick-1983")
1019	Oldham, M. et al., "A comparison of conventional 'forward planning' with inverse planning for 3D conformal radiotherapy of the prostrate," *Radiotherapy and Oncology*, 35:248-262 (1995) ("Oldham")
1020	Carol, M.P., *Chapter 2 – IMRT: Where we are today*, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 17-36 ("Carol-2")
1021	Carol, M.P., *Chapter 17 – Where we go from here: one person's vision*, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 243-252 ("Carol-17")
1022	Morrill, S.M. et al., "Treatment planning optimization using constrained simulated annealing," *Phys. Med. Biol.*, 36(10):1341-1361 (1991) ("Morrill-1991")

TABLE OF AUTHORITIES
(continued)

Page(s)

Exhibit No.	Description of Document
1023	*Reserved*
1024	Brooks, S.P., et al., "Optimization using simulated annealing," *The Statistician*, 44(2):241-257 (1995) ("Brooks-1995")
1025	Chen, G.T.Y. et al., Evaluation of Treatment Plans Using Dose Volume Histograms," *Front. Radiat. Ther. Onc.*, 21:44-55 (1987) ("Chen-1987")
1026	Neal, A.J. et al., "Comparison of treatment techniques for conformal radiotherapy of the prostate using dose-volume histograms and normal tissue complication probabilities," *Radiotherapy and Oncology*, 37:29-34 (1995) ("Neal-1995")
1027	Webb, S., "Optimization of conformal radiotherapy dose distributions by simulated annealing: 2. Inclusion of scatter in the 2D technique," *Phys. Med. Biol.*, 36(9):1227-1237 (1991) ("Webb-1991")
1028	Shalev, S. et al., "The Objective Evaluation of Alternative Treatment Plans: II. Score Functions," *Int. J. Radiation Oncology Biol. Phys.*, 20:1067-1073 (1991) ("Shalev-1991")
1029	Oldham, M. et al., "The optimization and inherent limitations of 3D conformal radiotherapy treatment plans of the prostate," *The British Journal of Radiology*, 68:882-893 (1995) ("Oldham-1995")
1030	Mohan, R., et al., "Clinically relevant optimization of 3-D conformal treatments," *Med. Phys.*, 19(4):933-944 ("Mohan-1992")

Petitioner Varian Medical Systems, Inc. ("Petitioner") respectfully submits this Petition for *Inter Partes* Review of claims 1 and 18 of U.S. Patent No. 6,393,096 ("the '096 patent") (Ex. 1001).

I. INTRODUCTION

The claims of the '096 patent challenged in this petition are nothing more than the obvious combination of features known and established within radiotherapy treatment planning prior art. The prior art disclosed, taught, and suggested all elements of the challenged claims. Since one of ordinary skill in the art would have been motivated to combine the prior art to meet all claim limitations with a reasonable expectation of success, the challenged claims are invalid.

Radiotherapy uses beams of radiation to treat tumors. Radiotherapy *planning* is the predetermined arrangement of beams (i.e., their number, orientations, and intensities) for a given patient's treatment. The aim of treatment planning is to determine the beam arrangement that supplies sufficient radiation to kill a tumor while minimizing the incident radiation exposure of the surrounding organs in accordance with dose limits prescribed by a physician.

The '096 patent is directed to the use of computer-implemented simulated annealing radiotherapy planning (SARP) in order to optimize the beam arrangement for a given dose prescription. Simulated annealing itself is a well-known numerical iterative optimization technique that can be used to minimize any type of "cost

function." In SARP, the cost function being minimized quantifies the "goodness of fit" between a given radiotherapy beam arrangement (i.e., the variable(s)) and a desired radiation dose prescription (i.e., the goal).

The '096 patent did not invent SARP. Rather, the '096 patent contends only to have invented new "cost functions" for use in SARP optimization. As the '096 patent admits, "[e]xcept for the foregoing detailed description of the cost function utilized in the present system, the details of the foregoing simulated annealing techniques are known in the art." (Ex. 1001 at 8:41-44.)

But, the cost functions allegedly invented and broadly claimed within claims 1 and 18 of the '096 patent were already established in the art. Their extensive disclosure and obvious use within SARP belies the scant references cited on the '096 patent and considered by the examiner during prosecution. Had the examiner been aware of the full scope of the prior art's extensive use of SARP and disclosed cost functions, the challenged claims would not have issued.

Specifically, the optimization method of claim 1 recites incorporating a cost function in order to "approach correspondence" between a cumulative dose volume histogram (CDVH) for a proposed beam arrangement and the CDVH of a dose prescription. But, this type of cost function was already known in the art and disclosed in the Viggars reference of Grounds 1 and 2 and the Carol-17 reference of Grounds 3 and 4.

Viggars expressly disclosed "score functions which compare the actual deviations of a plan from the ideal CDVH with the maximum deviations allowed by the dose prescription." (Viggars at 422.) Carol-17 discloses the use of "partial volume information for each structure out of which CDVH curves are generated and used as the goal by the optimizer." (Carol-17 at 247.)

As such, the grounds in this petition refute the '096 patent's assertion that the claimed cost functions were new. To the contrary, the claims are simply the obvious combination of the cost functions of Viggars or Carol-17 with the prior art SARP methods exemplified by Oldham (Grounds 1 and 2), Carol-2 (Grounds 3 and 4), and Morrill-1991 (Grounds 2 and 4).

Since there is a reasonable likelihood that Petitioner would prevail in demonstrating that claims 1 and 18 are obvious, the Board should institute an *Inter Partes* review of the '096 patent.

II. 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, 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 '096 patent is the subject of pending litigation involving the Petitioner, *Best Medical International, Inc. v. Varian Medical Systems, Inc.*, Case No. 1:18-cv-01599-MN (D. Del. Oct. 16, 2018), in which the patent owner contends that the Petitioner infringes the '096 patent. The Petitioner was served with a complaint in that action on October 18, 2018. The '096 patent has also been asserted in the cases *Best Medical International, Inc. v. Elekta AB et al.*, Case No. 1:18-cv-01600-MN (D. Del. Oct. 16, 2018) and *Best Medical International, Inc. v. Elekta Inc. et al.*, Case No. 1:19-cv-03409-MLB (N.D. Ga. July 28, 2019).

Petitioner is also submitting simultaneously herewith a petition requesting *Inter Partes* Review of claims 43, 44, and 46 of the '096 patent. Petitioner has submitted separate petitions for these claims because: (1) independent claims 1 and 43 are substantially different with respect to their scope, and share no similar claim elements except for their preambles and (2) Patent Owner may attempt to assert different priority dates for the different patent claims in an effort to overcome the grounds for invalidity in both Petitions. *See* Office Patent Trial Practice Guide July 2019 Update ("Practice Guide") at 26. Per the Board's current Practice Guide, if the Board uses its discretion to refuse to consider these separate Petitions on the merits, Petitioner ranks the present Petition challenging claims 1 and 18 of the '096 patent

above the simultaneously filed petition challenging claims 43, 44, and 46 of the '096 patent for consideration on the merits. *See id.*

Petitioner is also requesting *Inter Partes* Review of claims from U.S. Patent No. 6,038,283 ("the '283 patent"). Although the '096 patent is not technically related to the '283 patent, both patents share identical claim language, have substantially overlapping disclosures in their specifications, and have mostly overlapping inventors. Both were originally assigned to Nomos Corporation, and both have been assigned to present Patent Owner Best Medical International, Inc. The '283 patent has also been asserted by Patent Owner against Petitioner in the pending district court litigation. Furthermore, the terms identified for construction in the present Petition challenging the '096 patent have also been identified for construction by Petitioner with respect to the IPR Petition challenging claims of the '283 patent.

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

Heidi L. Keefe (Reg. No. 40,673) (lead) z/VarianBestIPRs@cooley.com zpatdcdocketing@cooley.com Cooley LLP ATTN: Patent Group 1299 Pennsylvania Ave. NW, Suite 700 Washington, DC 20004 Tel: (650) 843-5001 Fax: (650) 849-7400	Xiaozhen Yu (Reg. No. 75,031) z/VarianBestIPRs@cooley.com zpatdcdocketing@cooley.com Cooley LLP ATTN: Patent Group 1299 Pennsylvania Ave. NW, Suite 700 Washington, DC 20004 Tel: (202) 728-7127 Fax: (202) 842-7899

	Adam Pivovar (*Pro hac vice* application to be filed) z/VarianBestIPRs@cooley.com zpatdcdocketing@cooley.com Cooley LLP ATTN: Patent Group 1299 Pennsylvania Ave. NW, Suite 700 Washington, DC 20004 Tel.: (202) 842-7998 Fax: (202) 842-7899 Reuben Chen (*Pro hac vice* application to be filed) z/VarianBestIPRs@cooley.com zpatdcdocketing@cooley.com Cooley LLP ATTN: Patent Group 1299 Pennsylvania Ave. NW, Suite 700 Washington, DC 20004 Tel.: (650) 843-5480 Fax: (650) 849-7400

D. Service Information

Petitioner consents to electronic service at z/VarianBestIPRs@cooley.com.

III. PAYMENT OF FEES - 37 C.F.R. § 42.103

A payment of $30,500 is submitted herewith. This Petition meets the fee requirements of 35 U.S.C. § 312(a)(1).

IV. REQUIREMENTS FOR *INTER PARTES* REVIEW UNDER 37 C.F.R. §§ 42.104 AND 42.108

A. Grounds for Standing Under 37 C.F.R. § 42.104(a)

The Petitioner certifies that the ’096 patent is available for *inter partes* review, and that the Petitioner is not barred or otherwise estopped from requesting *inter*

partes review on the grounds identified in the present Petition. The Petitioner is unaware of any previous petition for *inter partes* review of the '096 patent.

B. Identification of Challenge Under 37 C.F.R. § 42.104(b) and Statement of Precise Relief Requested

Petitioner requests *inter partes* review of claims 1 and 18 and requests that the Board find the claims unpatentable under 35 U.S.C. § 103 (pre-AIA):

Ground	Claims	Basis of Invalidity
1	1	Obvious over Oldham in view of Viggars
2	18	Obvious over Oldham in view of Viggars and Morrill-1991
3	1, 18	Obvious over Carol-2 in view of Carol-17
4	18	Obvious over Carol-2 in view of Carol-17 and Morrill-1991

None of the references relied on in the foregoing grounds were before the examiner during prosecution.

This Petition is supported by the Declaration of Dr. Kenneth Gall, an expert with over 30 years of experience in the fields of radiation therapy and medical physics. (*See* Ex. 1002 (Gall Decl.) ¶¶1-12.)

C. Requirements for *Inter Partes* Review 37 C.F.R. § 42.108(c)

The Board should institute *inter partes* review of claims 1 and 18 because this Petition establishes a reasonable likelihood of prevailing with respect to each challenged claim. *See* 35 U.S.C. § 314(a).

V. BRIEF BACKGROUND OF THE UNDERLYING TECHNOLOGY

A. Conformal Radiotherapy

Radiation therapy (or "radiotherapy") generally involves the use of beams of radiation to treat tumors within a patient. (Webb-1993 at ix.) The goal of radiotherapy is "delivering a specified high dose to the target area [i.e., tumor] and as low a dose as possible elsewhere" in order to kill the diseased tissue while minimizing complications to otherwise healthy tissue and organs-at-risk (OARs) that the radiation beams pass through when directed onto the tumor. (*Id.* at 65.) This is known as "conformal radiotherapy," i.e., the high-dose conforms to the shape of the tumor. (*Id.* at 1.) It has long been known that conformal radiotherapy is most effective when it employs "multiple beams…from several directions to deliver a cumulative dose to the tumor volume" while distributing and thereby reducing the radiation dose to healthy organs. (Webb-1989 at 1349.)

Once a tumor volume is identified by an imaging method, the "ideal aim" of radiotherapy "would be to deliver a specified uniform dose to that area and to deliver zero dose elsewhere." (Webb-1993 at 65.) This is "clearly impossible since to reach the target area, photons must travel across surrounding tissue depositing dose *en route*." (Webb-1993 at 65.) In this regard, "it is well recognized that . . . normal tissue tolerance critically depends on the volume of irradiated tissue." (Lawrence-1990 at 1041; *see* Langer-1990 at 887 ("Organ tolerance . . . is better

predicted by the volume distribution of dose.").) Doctors therefore provide radiation dose prescriptions to meet the clinical objectives of applying sufficient radiation to kill a tumor while also specifying acceptable tolerated dose-volume limits on the surrounding healthy organs. (*See* Goitein-1992 at 247.)

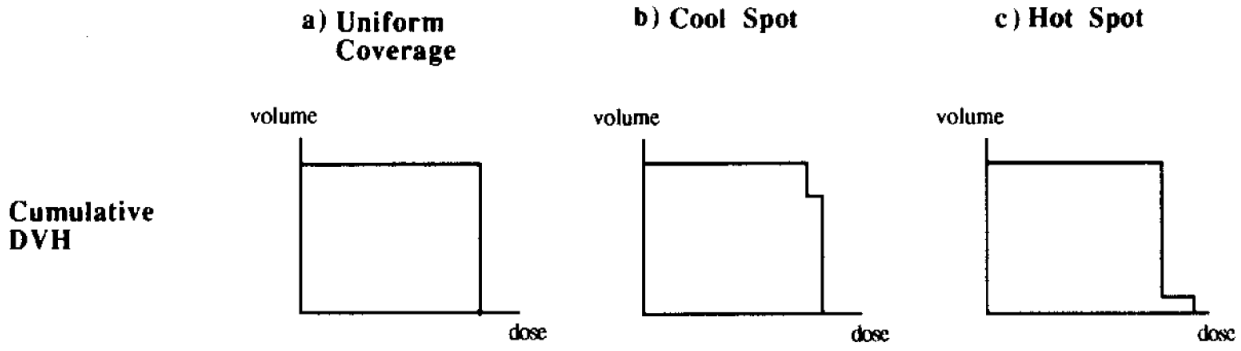
B. Radiotherapy Instruments

The radiation beams used for radiotherapy are typically supplied by "high-energy computer-controlled linear accelerators." (Morrill-1990 at 135.) These instruments have an adjustable patient table generally centered inside a rotatable gantry containing a beam shaping device or "collimator" to apply beams with different trajectories, intensities, and shapes that conform to the two-dimensional "beams-eye" view of the tumor at each trajectory. (Webb-1995 at 71.) As such, "treatment accelerators and beam collimators…can take up a large number of geometrical positions around the patient, under computer control, so as to tailor the high-dose region far better to the tumor" and minimize excessive radiation to healthy organs. (Webb-1989 at 1350.)

C. Cumulative Dose Volume Histogram (CDVH)

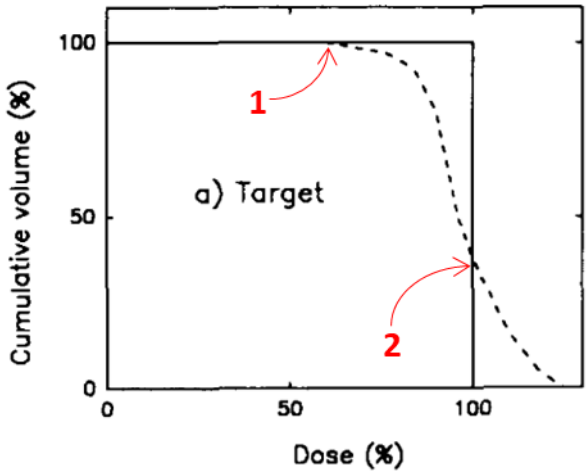
A cumulative dose-volume histogram ("CDVH") is a graphical representation of the cumulative amount of radiation received by a given volume of the target or an organ-at-risk for a radiation therapy beam arrangement. (Viggars-1992 at 419.) A CDVH is "V(D) plotted against D, where V(D) is the volume of tissue in which the

dose is greater than or equal to D." (*Id.*) Exemplary CDVHs of a target tumor volume corresponding to (a) uniform irradiation, (b) a small underdose (cool) region, and (c) a small overdose (hot) region are depicted as follows:



(Goitein-1992 at 252.)

An ideal dose prescription would be "uniform at 100% of the prescribed dose [in the target] and zero in all other tissues." (Viggars at 420.) The solid line in the image below depicts a CDVH associated with 100% of the target volume receiving 100% of the ideal dose prescription. (*Id.* at 421.) Because "[d]ose distributions which can be achieved in practice are less uniform in the target and are non-zero in normal tissue," the relative quality of a proposed beam arrangement to achieving a treatment objective may "be judged by how far its CDVH departs from the ideal" prescribed criteria. (*Id.* at 420-421.) As such, an optimal treatment plan is one which allows the greatest dose to the target according to the CDVH criteria prescribed by the doctor. (Lawrence-1990 at 1041-42.)



(*See* Viggars at 421 (annotated per Ex. 1002 ¶¶34-35).)

The interpretation of a CDVH is that a point on the CDVH represents the fractional volume of an anatomical structure (y-axis) that receives *at least* the dose identified on the x-axis. (Goitein-1992 at 251-252.) For example, in the dashed representation of a CDVH above, 100% of the target receives at least approximately 60% of the prescribed dose (annotated point 1), while approximately 40% of the target receives at least 100% of the prescribed dose (annotated point 2).

Dose-volume histograms "were first introduced precisely in order to compare treatment plans." (Goitein-1992 at 251; Drzymala-1991 at 77 ("Their greatest strength is their ability to provide rapid screening of plans.").) "Their acceptance has been rapid and widespread" and they are recognized as "an essential feature of a modern treatment planning system." (Goitein-1992 at 251, 253.)

Accordingly, CDVHs of tumor targets and surrounding organs have long been used by physicians to evaluate and compare the quality of different treatment plans

and their compliance with a desired radiation dose prescription. (Drzymala-1991 at 71.) CDVHs "may be used as a preliminary step in evaluating a treatment plan, or as a screening tool to select the best or most acceptable plan(s) from a group of plans." (*Id.*) CDVHs can be used to "evaluate the relative merit of treatment plans employing different field configurations" and "to estimate the partial organ tolerance of critical structures." (Chen-1987 at 44.) "They may also be used as a graphical way of comparing different treatment plans in a single plot, and . . . allowing quantitative scoring and evaluation of plans." (Drzymala-1991 at 71.)

D. Radiotherapy Therapy Treatment Planning

The flexibility provided by radiotherapy instruments has been "accompanied by advances in radiation therapy treatment planning—the process of selecting the proper patient position, radiation beams, and radiation doses required to treat the given patient." (Morrill-1990 at 135.) "An important problem in the construction of treatment plans employing multiple beams is the appropriate choice of relative beam exposures, or weights." (Langer-1990 at 887.) The choice of beam weights "determines the resulting distribution of dose within the treatment volume, upon which the probabilities of tumor cure and normal tissue complications ultimately depend." (*Id.*)

Historically, conventional treatment planning followed a trial-and-error approach in which "[t]he treatment planner chooses the free parameters" including

the beam orientations and amount of radiation provided at each beam trajectory (i.e., the beam weights). (Webb-1989 at 1350). After the beam arrangement parameters were selected, a "computer calculates the dose distribution." (*Id.*) The planner and therapist inspects the dose distributions for the target/tumor and surrounding organs for the beam arrangement "and then either accepts the arrangement of beams or modifies it until the prescription is met within limits." (*Id.*) This process can be referred to as *forward* treatment planning. (Webb-1995 at 71.)

It has long been known that a "more logical approach" to radiotherapy treatment planning "would be to start with the dose prescription and from this derive the beam arrangements." (Webb-1989 at 1350.) That is, "[g]iven a prescription of desired outcomes, compute the best beam arrangement." (Webb-1995 at 71.) This approach, called "inverse" or "reverse" treatment planning, forms "the basis of techniques which are generically known as optimization methods for treatment planning" (Webb-1989 at 1350) and requires that the optimization be "solved by a computer with human guidance rather than by human experience alone" (Webb-1995 at 71).

E. Optimization of Treatment Plans: Simulated Annealing Radiotherapy Planning (SARP)

Beginning in the 1980s, various computer-implemented optimization methods for inverse treatment planning have been developed. (*Id.* at 71-72.) The iterative

optimization method of simulated annealing is one such method used to optimize treatment plans, which has been called simulated annealing radiotherapy planning ("SARP"). (*Id.*)

Simulated annealing is a computer-implemented iterative optimization technique that has been utilized for solving optimization problems in a variety of different fields. (Webb-1989 at 1351.) The foundational implementation of simulated annealing optimization was demonstrated by Kirkpatrick in 1983. (*See id.* ("[t]he method of simulated annealing is attributed to Kirkpatrick *et al.* (1983)").) As its name suggests, simulated annealing is a numerical method that "mimics the way a thermalized system with a large number of degrees of freedom achieves its ground state as the temperature slowly decreases." (*Id.* at 1352.) That is, simulated annealing is a computer-implemented technique that determines "the global minimum of some function when the state-space of this function may possess multiple local minima." (Webb-1995 at 72.) The function used by a simulated annealing method is referred to as an "objective" or "cost" function. (*E.g.*, Webb-1989 at 1358; Kirkpatrick-1983 at 671.)

"Four ingredients" are needed to implement simulated annealing optimization of a multi-variable optimization problem: (1) a description of the configuration of the system; (2) a random generator of "moves" or rearrangements of the elements in a configuration; (3) a quantitative objective/cost function; and (4) an annealing

schedule that governs how the method probes the solution space in its attempts to minimize the cost function. (*See* Kirkpatrick-1983 at 679; *see also* Oldham-1995 at 884.)

In SARP, the optimization seeks to solve the inverse treatment planning problem—i.e., determining an optimal set of treatment beams (i.e., the variables) for delivering a tumorcidal dose of radiation to the tumor while delivering as small a dose of radiation to the normal tissue (i.e., the goal). (*See* Webb-1989 at 1349.) Accordingly, the cost function to be minimized in SARP "is a measure of fit between a dose distribution and some ideal, user-specified, dose distribution." (Oldham at 249.) "The minimum of the cost function defines the theoretical ideal dose distribution (and beam-weight set) which the optimization algorithm attempts to achieve." (*Id.* at 250.) "It is therefore critical that the cost function should reflect what is clinically desired in each different region of the patient." (*Id.*)

The cost functions used with SARP are simplified numerical approximations for the goal of determining a set of radiation beams that best deliver the treatment prescription. (Morrill-1990 at 136.) The "great power of simulated annealing lies in its flexibility" in that "[t]he cost function can be as simple or as complicated as one likes." (Webb-1995 at 74.) The outcome of the optimization can be tuned via the use of "importance" factors that weight the importance of different dose constraints in different regions within the patient—e.g., as between the tumor and

organs-at-risk—and by including constraints that must be satisfied (and not merely optimized). (Webb-1995 at 78; Morrill-1990 at 137.) The simulated annealing "optimization technique permits the straightforward utilization of any objective function and any set of dose constraints, even those described by non-analytic functions." (Morrill-1990 at 135.)

Determining an optimal beam arrangement with SARP involves iteratively evaluating various beam arrangements to find one that minimizes a cost function that quantifies compliance with the treatment objectives. (*See, e.g.*, Webb-1995 at 72.) SARP optimization thus begins with an initial configuration of radiation beams of different trajectories and intensities. (*E.g.*, Morrill-1990 at 139 (Fig. 1).) The cost function is used to calculate the "cost" of the initial beam configuration. (*Id.*) The initial beam configuration is randomly changed to a new configuration—typically by changing the beam "weight"—and a new value for the cost function is calculated. (*Id.*) The initial and new costs are compared and the change is either accepted or rejected. (*Id.*) If the cost has decreased by changing the beam configuration, the new (changed) configuration is accepted and becomes the current configuration. (*Id.*) If the cost has increased, the change is usually rejected and, if so, the initial configuration remains the current configuration. (*Id.*) The current beam arrangement then becomes the baseline for the next iteration, and the steps are

repeated until minimization of the cost function achieves an "optimal" beam configuration. (*Id.*)

VI. SUMMARY OF THE '096 PATENT

A. The Specification and File History of the '096 Patent

The '096 patent is entitled "Planning Method and Apparatus for Radiation Dosimetry." (Ex. 1001.) The "Background of The Invention" section of the '096 patent includes a "Description of the Prior Art." (Ex. 1001 at 1:13-4:9.) The '096 patent admits that conformal radiation therapy "has two goals: eradication of the tumor and avoidance of damage to healthy tissue and organs present near the tumor." (Ex. 1001 at 1:14-16.) The patent further acknowledges that conformal radiotherapy "typically uses a linear accelerator ('LINAC') as the source of the radiation beam used to treat the tumor" (Ex. 1001 at 1:28-31), and describes the known use of multileaf collimators and beam intensity modulation for delivering conformal radiation beams. (Ex. 1001 1:35-3:5.)

The '096 patent admits that the "[e]xisting methods and apparatus for optimizing treatment plans use a computer to rate possible plans based on score functions which simulate a physician's assessment of a treatment plan." (Ex. 1001 at 3:12-15.) The '096 patent explains that "[o]ne such computational method is known in the art as simulated annealing." (Ex. 1001 at 3:21-22.) "Simulated annealing radiotherapy planning ('SARP') methods are well known in the art to

compute optimized radiation beam arrangements to meet objective parameters of a physician with regard to conflicting treatment objectives of a tumor volume and its surrounding structures." (Ex. 1001 at 5:3-7.) Furthermore, the '096 patent explains that the "[e]xisting SARP methods utilize systematic algorithms to calculate a proposed, optimized beam arrangement." (Ex. 1001 at 5:7-9.) "Ultimately, the SARP method will produce an optimized treatment plan, based on the treatment objectives as expressed by the cost function incorporated in the SARP algorithm." (Ex. 1001 at 5:50-53.)

The '096 patent contends that "the cost functions used in existing methods do not account for the structure volumes as a whole, relying merely on costs related to discrete points within the structure, and further do not account for the relative importance of varying surrounding structure types." (Ex. 1001 at 3:25-30.) According to the '096 patent, "[e]xisting cost functions utilized in the optimization of treatment plans do not account for such varying costs associated with the different types of structures." (Ex. 1001 at 3:38-40.) The '096 patent then contends that "prior to the development of the present invention, there has been no method or apparatus for conformal radiation therapy" which utilizes partial volume data or the associated "CDVH curves in establishing the desired dose distributions for each target tumor volume and tissue and structure types." (Ex. 1001 at 3:53-65.)

The ’096 patent alleges to have disclosed “an improved optimized treatment planning system” that “includes a modified cost function, which allows a physician to use conventional cumulative dose volume histographs (CDVH’s) to establish a desired prescription of dosage to both the target volume, or target, and each involved structure volume.” (Ex. 1001 at 5:54-61.) The ’096 patent does not purport to have invented the use of simulated annealing for radiotherapy planning (SARP). Rather, the ’096 patent asserts to have invented the use of allegedly “new” cost functions to be used with the well-known SARP optimization methods:

> [T]he radiation plan optimization is a specific case of an inverse problem, where the goal is to determine the best way to achieve the dose prescription. ***A SARP technique is utilized to do this optimization*** . . . . ***Except for the foregoing detailed description of the cost function utilized in the present system, the details of the foregoing simulated annealing techniques are known in the art*** . . . .

(Ex. 1001 at 8:34-44 (emphasis added).)

After an optimized treatment plan is calculated by the SARP algorithm, the physician reviews the plan prior to “approv[ing] the radiation plan for patient delivery.” (Ex. 1001 at 15:63-65, Fig. 2 (Step 806).)

During prosecution, the examiner allowed all claims as originally submitted without rejection. (Ex. 1005, September 7, 2000 Notice of Allowability.) The reasons for allowance provided by the examiner were as follows:

> [T]he claims address a method and apparatus of determining an optimized radiation beam arrangement for applying radiation to a tumor target where correspondence of a proposed beam arrangement with a CDVH is used and the radiation beam intensity is increased or decreased if the change leads to greater correspondence, or a CDVH is used as part of an iterative algorithm using a cost function to calculate correspondence of partial volume data associated with the proposed radiation beam arrangement with the partial volume data associated with the desired dose prescription . . . . This feature is neither shown nor fairly suggested in the prior art.

(*Id.*)

VII. THE LEVEL OF ORDINARY SKILL IN THE ART

A person of ordinary skill in the art of the '096 patent as of May 1997 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. A person could also have qualified as a person of ordinary skill in the art with some combination of (1) more formal education and less technical experience or (2) less formal education and more technical or professional experience in the fields listed above. (Ex. 1002 ¶16.)

VIII. STATEMENT OF MATERIAL FACT

The following statement of material fact is authorized by 37 C.F.R. §42.22(c). Patent Owner must admit, deny, or state why it cannot admit or deny each statement of material fact. 37 C.F.R. §42.23(a).

1. Except for the detailed description of the cost function disclosed in the '096 patent, the details of simulated annealing radiotherapy planning (SARP) techniques were known in the art and would have been within the knowledge of a person of ordinary skill in the art, as stated in the '096 patent at 8:41-44.

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

A claim subject to *inter partes* review must be construed "[i]f a petitioner believes that a claim term requires an express construction." *See* Practice Guide at 13. "On the other hand, a petitioner may include a statement that the claim terms require no express construction." *Id.*

Means-plus-function claiming occurs when a claim term is drafted in a manner that invokes 35 U.S.C. 112 ¶ 6. *See Williamson v. Citrix Online, LLC*, 792

F.3d 1339, 1347 (Fed. Cir. 2015) (en banc). If a claim challenged in an IPR petition contains a means-plus-function limitation, the petition "must identify the specific portions of the specification that describe the structure, material, or acts corresponding to each claimed function." 37 C.F.R. § 42.104(b)(3); *see also* Practice Guide at 13.

For purposes of this Petition, Petitioner identifies the following terms for construction. For claim terms not addressed below, Petitioner has applied the plain and ordinary meaning of those terms to a POSA.

A. "a computer to computationally obtain a proposed radiation beam arrangement"

The claim term "a computer to computationally obtain a proposed radiation beam arrangement" is drafted in means-plus-function format and subject to construction under 35 U.S.C. § 112 ¶ 6 under Federal Circuit precedent. "[M]erely because an element does not include the word 'means' does not automatically prevent that element from being construed as a means-plus-function element." *Williamson*, 792 F.3d at 1348. Rather, when a claim term lacks the word "means," 35 U.S.C. 112 ¶ 6 applies "if the challenger demonstrates that the claim term fails to 'recite[] sufficiently definite structure' or else recites 'function without reciting sufficient structure for performing that function.'" (*Id.*)

Here, a POSA would not understand the words "a computer to computationally obtain a proposed radiation beam arrangement" to have a sufficiently definite meaning as the name for structure. (Ex. 1002 ¶60.) The term simply recites a generic "computer" for performing the specialized-computer implemented function of computationally obtaining a proposed radiation beam arrangement. (*Id.*) Such "black box" general-purpose-computer-implemented functional claiming is construed under § 112 ¶ 6. *See Williamson,* 792 F.3d at 1350 (construing "distributed learning control module" as a means-plus-function element because "'module' is simply a generic description for software or hardware that performs a specified function"); *Blackboard, Inc. v. Desire2Learn, Inc.*, 574 F.3d 1371, 1383 (Fed. Cir. 2009) (concluding that claim term "access control manager" is "simply an abstraction . . . performed by some undefined component of the system" and that it is "essentially a black box that performs a recited function"); *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1367 (Fed. Cir. 2008) (construing the term "bank computer" as a means-plus-function element).

The term is also drafted in a format consistent with traditional means-plus-function claim limitations, merely using the recitation of "computer" instead of "means" for performing the function of computationally obtaining a proposed radiation beam arrangement. *See Williamson,* 792 F.3d at 1350 (construing "distributed learning control module" as a means-plus-function element because it

simply "replaces the term 'means' with the term 'module,'" a "nonce" word). Accordingly, the term "a computer to computationally obtain a proposed radiation beam arrangement" recited in claim 1 is subject to means-plus-function claim construction under § 112 ¶ 6. (Ex. 1002 ¶60.)

Claim construction of a means-plus-function limitation includes two steps. *Applied Med. Res. Corp. v. US Surgical Corp.*, 448 F.3d 1324, 1332 (Fed. Cir. 2006). First, the court must determine the claimed function. *JVW Enters. v. Interact Accessories, Inc.*, 424 F.3d 1324, 1330 (Fed. Cir. 2005). Second, the court must identify the corresponding structure in the written description of the patent that performs that function. *Id*.

"If special programming is required for a general-purpose computer to perform the corresponding claimed function, then the default rule requiring disclosure of an algorithm applies." *Ergo Licensing, LLC v. CareFusion 303, Inc.*, 673 F.3d 1361, 1365 (Fed. Cir. 2012); *see also Harris Corp. v. Ericsson Inc.*, 417 F.3d 1241, 1249 (Fed. Cir. 2005). "In a means-plus-function claim in which the disclosed structure is a computer, or microprocessor, programmed to carry out an algorithm, the disclosed structure is not the general purpose computer, but rather the special purpose computer programmed to perform the disclosed algorithm." *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1349 (Fed. Cir. 1999).

For the term "a computer to computationally obtain a proposed beam arrangement," the *claimed function* is "computationally obtaining a proposed radiation beam arrangement." (Ex. 1002 ¶62.)

The only algorithm a POSA would recognize within in the specification for "computationally obtaining a proposed radiation beam arrangement" is a SARP optimization algorithm. (Ex. 1002 ¶63.) The specification explains that the "[e]xisting SARP methods utilize systematic algorithms to calculate a proposed, optimized beam arrangement" and that "the SARP method will produce an optimized treatment plan, based on the treatment objectives as expressed by the cost function incorporated in the SARP algorithm." (Ex. 1001 at 5:7-9, 5:50-53.) The specification further discloses, at 8:34-59, that "[a] SARP technique is utilized to do this optimization by dividing the radiation delivery into a large number of small beams, each of which hit the target" and "[e]xcept for the foregoing detailed description of the cost function utilized in the present system, the details of the foregoing simulated annealing techniques are known in the art." (Ex. 1001 at 8:41-44.) The specification also states that "[a] suitable computer is utilized in performing the Plan Optimization step." (Ex. 1001 at 8:52-59.)

A POSA would therefore recognize that the *corresponding structure* for performing the claimed function is "a computer programmed with a simulated annealing radiotherapy planning (SARP) optimization algorithm according to the

disclosure at 8:34-59 that generates a radiation beam arrangement used as input for subsequent optimization, and equivalents thereof." (Ex. 1002 ¶64.)

B. "a computer to computationally change the proposed radiation beam arrangement iteratively"

The claim term "a computer to computationally change the proposed radiation beam arrangement iteratively" is drafted in means-plus-function format and must be construed pursuant to 35 U.S.C. § 112 ¶ 6. As with the previous claim term, the phrase "a computer to computationally change the proposed radiation beam arrangement iteratively" is a general-purpose computer-implemented functional claim term that does not connote sufficiently definite structure to a person of ordinary skill in the art, and the presumption against means-plus-function claiming is also overcome. (*See* Ex. 1002 ¶65.)

The *claimed function* for this term is "computationally changing the proposed radiation beam arrangement iteratively." (Ex. 1002 ¶66.) A POSA would recognize that SARP methods include an algorithm that performs the claimed function as part of the overall SARP iterative optimization techniques disclosed in the specification. (Ex. 1002 ¶67.) The '096 patent explains, at 8:34-59, that in the "Plan Optimization step," "[a] SARP technique is utilized" and that "[e]xcept for the foregoing detailed description of the cost function utilized in the present system, the details of the foregoing simulated annealing techniques are known in the art. . . ." (Ex. 1001 at

8:34-59.) The specification also discloses that "[t]he optimal beam arrangement is arrived at by computationally increasing the beam weight iteratively" and that "[u]ltimately, the SARP method will produce an optimized treatment plan." (Ex. 1001 at 5:39-53.)

A POSA would understand that random changes to the beam parameters at each iteration is an inherent and defining characteristic of a SARP optimization algorithm. (Ex. 1002 ¶68; *E.g.*, Neal-1995 at 30 ("this iterative algorithm randomly perturbs the beam-weights"); Oldham-1995 at 249 ("at each iteration all beam-weights are independently perturbed by adding a 'grain' of beam-weight which is selected randomly;" "[t]he grains are randomly positive or negative"); Morrill-1991 at 1343 ("This solution is then randomly altered").) Accordingly, the *corresponding structure* for the claimed function is "a computer programmed with a simulated annealing radiotherapy planning (SARP) optimization algorithm according to the disclosure at 8:34-59 that randomly changes the beam arrangement at each iteration, and equivalents thereof."

C. Invalidity Based on the Board's Claim Construction

If the Board concludes that the foregoing computer-implemented functional claim terms are not drafted in means-plus-function format, then Petitioner contends that no construction for the terms is required. The grounds identified herein will remain sufficient to demonstrate the invalidity of the patent claims under the

ordinary meaning of these terms because each ground identifies a computer to perform the recited computer-implemented functions.

X. PRIORITY DATE FOR THE CLAIMS OF THE '096 PATENT

The '096 patent application was filed on May 27, 1999 and claims priority to provisional application 60/087,049, filed on May 27, 1998. It is Patent Owner's burden to demonstrate entitlement to the provisional filing date and/or an earlier date of invention. For purposes of this petition, Petitioner's grounds are based on prior art that predates the absolute 102(b) date of May 27, 1997, and the 102(a) provisional filing date of May 27, 1998.

XI. GROUND 1: CLAIM 1 IS OBVIOUS OVER OLDHAM IN VIEW OF VIGGARS

A. Prior Art and Date Qualification

Each limitation of claim 1 is disclosed, taught, or suggested by the combination of Oldham *et al.*, *A comparison of conventional 'forward planning' with inverse planning for 3D conformal radiotherapy of the prostate*, Radiotherapy and Oncology 35 (1995) 248-262 **("Oldham")** (Ex. 1019) and Viggars *et al.*, *The objective evaluation of alternative treatment plans III: the quantitative analysis of dose volume histograms*, Int. J. Radiation Oncology Biol. Phys. (23) 419-427 (1992) **("Viggars")** (Ex. 1015).

Both Oldham and Viggars are § 102(b) prior art, as established by library date stamps. (Ex. 1003 (Hall-Ellis Decl.) ¶¶54-59, 65-70.) Both are over 20 years old,

therefore qualifying as ancient documents, and were published in well-known, reputable scientific journals. (Ex. 1002 ¶73.) Neither Oldham nor Viggars was before or considered by the Examiner during prosecution.

B. Brief Description of Oldham [Ex. 1019]

Oldham discloses a fast simulated annealing method for optimizing a treatment plan that uses "a cost-function designed to achieve a homogenous dose in the 'planning-target-volume' and to minimize the integral dose to the organs at risk." (Oldham at 248 (Abstract).) The cost function was segmented into component terms for the target, organs-at-risk, and normal body tissue. (*Id.* at 250.) Each term within the cost function "was weighted by an 'importance factor' to define its relative importance at the start of the optimization." (*Id.*) Oldham concluded that "[i]n practice it was found surprisingly easy to find a practical set [of importance factors] that gave good dose distributions." (*Id.* at 253.)

C. Brief Description of Viggars [Ex. 1015]

Viggars discloses a computer program ("OSCAR") for evaluating dose-volume histograms for use in 3-dimensional treatment planning. (Viggars at 419.) Viggars is the third paper in a series of publications by the authors related to "The Objective Evaluation of Alternative Treatment Plans." (Ex. 1002 ¶76.) The computer program first "uses a dose prescription which summarizes the radiation oncologist's perception of the treatment requirements for a patient or group of

patients." (Viggars at 420.) Table 1 of Viggars provides a representative dose-volume prescription used by the OSCAR computer program:

Table 1. Dose prescription for treatment of ca lung

Type of regret	Dose limit (%)	Maximum volume* (%)
Target overdose (severe)	110	20
Target overdose (mild)	105	50
Target under overdose (severe)	90	5
Target under overdose (mild)	95	50
Non-target overdose	95	100
Left lung	50	30
Right lung	50	30
Spinal cord	75	0

(*Id.* at 421.)

The following components are used by the computer program for analyzing a proposed dose distribution: "a) images of regret on multiple CT slices…, b) a visual display of the prescribed dose-volume limits on the CDVH, c) objective score functions which quantify the deviation of the dose distribution from the dose prescription, d) histograms of regret in either cumulative or differential form, which provide a striking and easily assimilated visual comparison of the CDVH or DDVH with the dose prescription." (*Id.* at 420.) In this context, "regret" is the deviation from the criteria in the dose prescription. (Shalev-1991 at 1067.)

The quality of a proposed treatment is "judged by how far its CDVH departs from the ideal histograms." (Viggars at 420.) Specifically, Viggars uses

mathematical "score" functions as "a quantitative measure of how well a proposed treatment plan conforms to the dose prescription" by "compar[ing] the actual deviations of a plan from the ideal CDVH with the maximum deviations allowed by the dose prescription." (*Id*. at 422.) Viggars expressly teaches that "***an optimal plan could, in principle, be selected by assigning weights to each score to derive an overall cost function***." (*Id.* at 425 (emphasis added).)

The application of the score functions in Viggars to quantitatively assess rival treatment plans "is demonstrated by applying it to the evaluation of alternative volumetric treatment plans for ca lung" (*id*. at 419 (Abstract)) according to the following iterative process (*id.* at 426 (Fig. 7)):

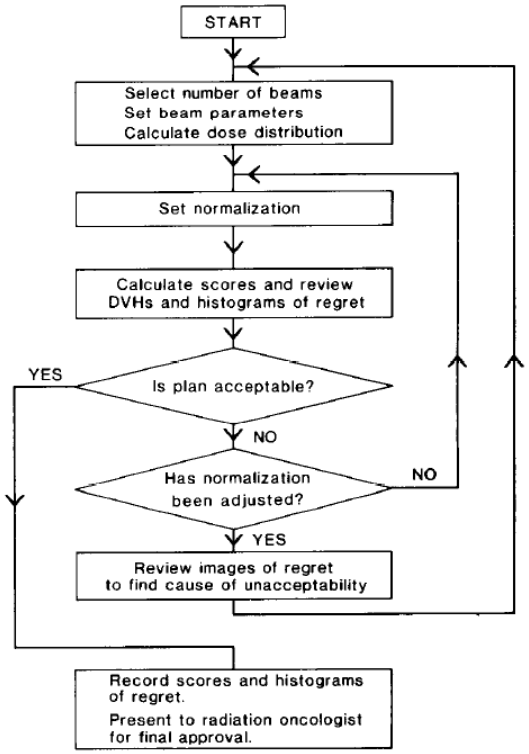
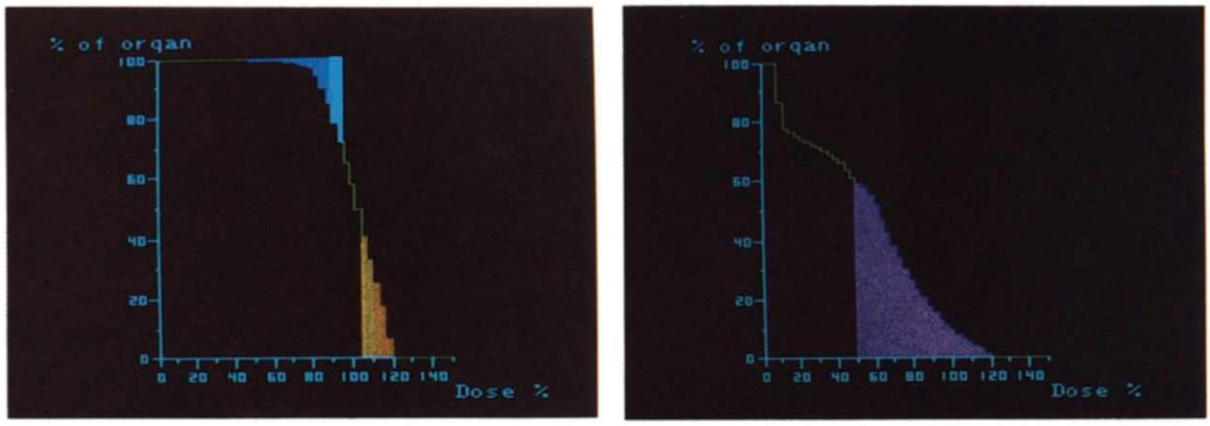


Fig. 7. Flow chart to illustrate the application of OSCAR techniques to treatment planning.

Deviations between the CDVHs of a treatment plan and the ideal dose prescription for the target and organs-at-risk can be depicted by Viggars' OSCAR program, as exemplified in the following images:



(c) (d)

(*Id.* at 422 (Fig. 3).)

D. Motivation to Combine and Reasonable Expectation of Success

Oldham and Viggars are in the same field and both are directed to using computer-implemented algorithms with cost (or "score") functions to quantitatively identify preferred beam arrangements for conformal radiotherapy. (Ex. 1002 ¶84.) It was well known prior to the filing of the '096 patent that physicians regularly used CDVHs for "evaluating a treatment plan, or as a screening tool to select the best or most acceptable plan(s)." (Drzymala-1991 at 77 ("Their greatest strength is their ability to provide rapid screening of plans.").) The specification of the '096 patent itself admits that "[p]hysicians and those skilled in the art of radiation dosimetry are familiar with desired CDVH curves" and that "CDVH curves . . . are typically used

by a physician in reviewing the effect a given dose distribution will have on a target or structure before that dose distribution is applied to the patient." (Ex. 1001 at 6:41-6:46.) Viggars expressly supports the motivation to use CDVH-based evaluation criteria for treatment planning: "DVH's are extremely useful in the initial stages of comparing and evaluating alternative plans and are increasingly being used in external beam radiotherapy planning." (Viggars at 419.)

The prior art acknowledged that Viggars "addressed the problem of basing a decision on the degree of acceptability of a treatment plan in terms of simple parameters." (Webb-1993 at 20.) In doing so, Viggars expressly discloses and suggests using an overall CDVH-based cost function to determine an optimal treatment plan: "***an optimal plan could, in principle, be selected by assigning weights to each score to derive an overall objective function***." (Viggars at 425 (emphasis added).) Oldham teaches how to determine suitable weights for the individual costs associated with an overall cost function. (Oldham at 253.) Accordingly, a POSA would have been motivated by Oldham to construct and incorporate the overall cost function disclosed in Viggars within Oldham's optimization algorithm. (Ex. 1002 ¶85.)

It was well known that in an optimization algorithm "[t]he cost function is a measure of fit between a dose distribution and some ideal, user-specified, dose distribution." (Oldham at 249.) A person of ordinary skill in the art also would have

been motivated to use the cost function expressly disclosed in Viggars in order to perform computer-implemented optimization of a treatment plan of Oldham to implement the same CDVH-based evaluations of proposed treatment plans that were already being performed by the physician. (Ex. 1002 ¶87.) Doing so simply incorporates the physician's evaluation criteria into the computer-implemented optimization with the benefit of guiding the determination of computer-optimized treatment plans towards beam configurations that are more likely to satisfy a physician's ultimate evaluation of the desired dose distribution. (*Id.*)

Optimization using the CDVH-based cost function of Viggars also has the clear motivating benefit of being able to effectively and efficiently screen a vast set of different beam configurations with the SARP algorithm of Oldham to arrive at a more optimal treatment configuration that could not otherwise be evaluated by a human physician on a configuration-by-configuration basis. (Ex. 1002 ¶88.) Viggars expressly discloses this automated optimization motivation: "most of the work in selecting and improving a treatment plan can be done without the ongoing intervention of a radiation oncologist, since his or her requirements have been specified in advance in the dose prescription." (Viggars at 425; Ex. 1002 ¶88.)

A POSA would also have been motivated to incorporate the overall cost function of Viggars in the SARP algorithm of Oldham to account for admitted shortcomings in the cost function used by Oldham. (Ex. 1002 ¶88.) Oldham states

that the cost function utilized therein is "of simple design, without the sophistication to model complicated volume effects." (Oldham at 250.) A POSA would understand that the CDVH-based cost function of Viggars would overcome the shortcoming of Oldham's cost function, as Viggars' CDVH-based cost function accounts for dose-volume limits associated with partial volumes identified in the physician's dose prescription. (Ex. 1002 ¶88.)

A POSA would further have been motivated to combine the score functions of Viggars into a single overall cost function because "a single figure of merit for a treatment plan would perhaps be easier to interpret than the full set of scores" for the target, organs, and tissue. (*Id*. at 426; Ex. 1002 ¶89.) Because "this would require a system of weighting the different scores for the target, non-target tissue and specific dose-limiting organs," Viggars suggests "allowing the clinician to make a final decision on their relative importance in accordance with the needs of individual patients." (*Id*.) This is synonymous with the recommendation of Shalev-1991, which is the second article in the series of Viggars publications entitled "The Objective Evaluation of Alternative Treatment Plans: II. Score Functions" and explicitly suggests that the task of weighing the different score functions within an overall cost function "is left to the clinician responsible for the management of the patient's treatment." (Shalev at 1068; Ex. 1002 ¶89.)

Additionally, Oldham's teaching of how to assign suitable weights to the individual components would have made it obvious to try the overall CDVH-based cost function suggested by Viggars with Oldham's SARP algorithm in order to determine an "optimal plan." (Ex. 1002 ¶92.)

A POSA would have reasonably expected success in using the overall cost function of Viggars with the SARP algorithm of Oldham. (Ex. 1002 ¶90.) First, a POSA would have understood that one of the benefits of simulated annealing optimization methods is that it "permits the straightforward utilization of any objective function . . . even those described by non-analytic functions." (Morrill-1990 at 135.) Thus, a POSA would understand that Viggars' overall cost function could be used in lieu of Oldham's cost function. (Ex. 1002 ¶90.)

Second, a POSA would have reasonably expected to successfully identify weights to be applied to the target, organs, and tissue to arrive at an overall CDVH-based cost function that could be minimized by the Oldham SARP algorithm. (Ex. 1002 ¶91.) Each component—i.e., target, organ, tissue—of the total cost function in Oldham "was weighted by an 'importance factor' to define its relative importance at the start of the optimisation." (Oldham at 250.) A POSA would have understood that "there is an 'intuitive' correspondence between the importance factors and the resulting dose distribution." (Oldham-1995 at 887.) Oldham also provides guidance on how a POSA would determine suitable weight/importance factors by making

"informed importance factor set 'guesses,'" which were then evaluated using a trial-and-error approach. (Oldham at 253; Ex. 1002 ¶92.) Oldham demonstrated that "***[i]n practice it was found surprisingly easy to find a practical set that gave good dose distributions***" as a suitable set "was arrived at after three 'guesses.'" (*Id*. at 253 (emphasis added).)

For example, a POSA would have recognized that treatment plans that only involve a single target, a single organ-at-risk, and the normal tissue would only require three weighting factors, and that finding three suitable weighting factors for Viggars CDVH-based overall cost function would have been straightforward in view of the teachings of Oldham. (Ex. 1002 ¶94.) A POSA would have further known that there were no hardware limitations that would have prevented implementation of the combination of Oldham and Viggars, as outlined above. (*Id.*)

Accordingly, one of skill in the art would have been motivated to replace the cost function of Oldham with the overall CDVH-based cost function of Viggars and would have possessed the ability to implement the combination with a reasonable expectation of success. (Ex. 1002 ¶95.)

E. Claim 1

Claim 1 is obvious over the combination of Oldham and Viggars. Claim 1 is an open "comprising" claim that has no requirements regarding the number of iterations, any specific threshold level of "optimization" achieved by the claimed

method, or the speed with which such optimization can be performed, and can be satisfied by a simple treatment plan with a dose prescription for one "target," one "structure," and the surrounding normal tissue. (Ex. 1002 ¶96.)

Each element of method claim 1 is disclosed, taught, or suggested by the teachings of Oldham incorporating the overall CDVH-based cost function disclosed in Viggars that "compare[s] the actual deviations of a plan from the ideal CDVH," as demonstrated in the following sections. (Ex. 1002 ¶96.) Since there was a motivation to combine Oldham and Viggars with a reasonable expectation of success in satisfying all elements of claim 1, the claim is obvious.

1. "A method of determining an optimized radiation beam arrangement for applying radiation to a tumor target volume while minimizing radiation of a structure volume in a patient, comprising the steps of:" (Preamble)

To the extent the preamble is limiting, it is disclosed by Oldham. (Ex. 1002 ¶97.) Oldham teaches a fast simulated annealing optimization method for treatment planning, which uses "a cost-function designed to achieve a homogenous dose in the 'planning-target-volume' and to minimise the integral dose to the organs at risk." (Oldham at 248.) The method "is employed to find the set of beam-weights that corresponds to the minimum of a cost function." (*Id*. at 249.) "Twelve patients were used in the study," and as a result, the treatment plan optimization algorithm "has

been applied to 48 prostate plans." (*Id*. at 248.) Thus, Oldham teaches this limitation.

Oldham's relevant disclosures of the preamble would not be altered by incorporating the overall cost function of Viggars with Oldham's SARP optimization algorithm. (Ex. 1002 ¶98.) The CDVH-based cost function of Viggars is "a convenient objective technique for characterizing, comparing and evaluating DVH's which uses a simple dose prescription provided by a radiation oncologist based on clinical experience and dose response data." (Viggars at 420.) Viggars discloses overdose and underdose limits for the radiation applied to the target, as well as dose-volume limits on the radiation received by the organs-at-risk and non-target tissue. (Ex. 1002 ¶98; Viggars at 420-421.) Accordingly, the combination of Viggars overall cost function with Oldham "determin[es] an optimized radiation beam arrangement for applying radiation to a tumor target volume while minimizing radiation of a structure volume in a patient." (*Id.*)

2. "using a computer to computationally obtain a proposed radiation beam arrangement;" (1[a])

Oldham describes a computer program, COVIRAOPT, developed under the "COVIRA (Computer Vision in Radiology)" program of the European Union. (Oldham at 261.) The program uses a fast simulated annealing algorithm and "at each iteration all beam-weights are independently perturbed . . . ." (*Id*. at 249.) "In

this manner the algorithm finds beam-weight sets that successively converge to that set which corresponds to the minimum of the cost function." (*Id.*)

Oldham's use of a computer-implemented fast simulated annealing algorithm performs the claimed function of computationally obtaining a proposed radiation beam arrangement by proposing new beam weights at each iteration of the optimization process. (Ex. 1002 ¶100.) The corresponding structure is satisfied by Oldham because fast simulated annealing is a SARP algorithm and the proposed beam weights are used as input for subsequent optimization. (*Id.*) Accordingly, claim element 1[a] is disclosed by Oldham.

If the Board concludes that the computer-implemented function of claim element 1[a] is not drafted in means-plus-function format, Oldham's use of a computer to perform fast simulated annealing to propose new beam weights at each iteration, as identified above, satisfies the claim limitation. (Ex. 1002 ¶101.)

3. "using a computer to computationally change the proposed radiation beam arrangement iteratively," (1[b])

The computer used in Oldham implements an iterative fast simulated annealing algorithm and explains that "[i]n this iterative method, at each iteration all beam-weights are independently perturbed by adding a 'grain' of beam-weight which is selected randomly from a Cauchy distribution." (Oldham at 249.) "The grains are randomly positive or negative and hence individual beam-weights can

independently increase or decrease . . . ." (*Id*.) Dependent claim 32 recites "wherein the proposed radiation beam arrangement is changed by changing the beam weights," therefore indicating that a change in the "beam weight" is necessarily a change in the "beam arrangement." (Ex. 1001 at 19:65-67; Ex. 1002 ¶102.) Therefore, Oldham discloses this claim element, including both the claimed computer-implemented function and corresponding structure in the form of the computer programmed with the fast simulated annealing algorithm that randomly changes the beam weights at each iteration. (Ex. 1002 ¶102.)

If the Board concludes that the computer-implemented function of claim element 1[b] is not drafted in means-plus-function format, Oldham's use of a computer to perform fast simulated annealing to change the beam weights at each iteration, as identified above, satisfies the claim limitation. (Ex. 1002 ¶103.)

4. "incorporating a cost function at each iteration to approach correspondence of a CDVH associated with the proposed radiation beam arrangement to a CDVH associated with a predetermined desired dose prescription;" (1[c])

Oldham's optimization algorithm incorporating Viggars' overall CDVH-based cost function satisfies this claim element. (Ex. 1002 ¶104.) Oldham teaches that "[t]he numerical method used to find the cost-function minimum was fast simulated annealing." (Oldham at 249.) At each iteration, "all beam-weights are independently perturbed by adding a 'grain' of beam-weight" and the cost function

"is evaluated for the current beam-weight set and compared to the running cost-function value (*i.e.*, the lowest cost-function value found from previous iterations)." (*Id.*) Eventually, "the algorithm finds beam-weight sets that successively converge to that set which corresponds to the minimum of the cost function." (*Id.*)

Oldham uses a total cost function that is segmented into component terms for each of the target (PTV), organs-at-risk (OAR), and surrounding tissue (BODY). (*Id.* at 250.) The component terms "were merged linearly to form the total cost function." (*Id.*) "Each term was weighted by an 'importance factor' to define its relative importance at the start of the optimisation." (*Id.*) The mathematical representation of Oldham's cost function (C_{TOTAL}) is provided below, with PTV, OAR and BODY standing for the planning target volume, organ-at-risk, and all tissue that is not in the PTV or OAR, respectively.

$$C_{TOTAL}(n) = \mathrm{WEIGHT}_{PTV} \times C_{PTV}(n)/C_{PTVST}(1) + \sum_{j=1}^{m} (\mathrm{WEIGHT}_{OAR_j} \times C_{OAR_j}(n)/C_{OARST_j}(1)) + \mathrm{WEIGHT}_{BODY} \times C_{BODY}(n)/C_{BODYST}(1) \quad (5)$$

(*Id.*)

It would have been obvious to a POSA to incorporate the segmented score functions of Viggars for the target, organs-at-risk, and non-target tissue into an overall cost function that replicates the merged and weighted total cost function of

Oldham. (Ex. 1002 ¶107.) Viggars expressly teaches that the "[s]cores are calculated, and an optimal plan could, in principle, be selected by assigning weights to each score to derive an overall objective function" (Viggars at 425) and the Oldham algorithm would serve "to find the set of beam weights that corresponds to the minimum of a cost function" (Oldham at 249).

Viggars' overall cost function satisfies claim element 1[c] because the segmented score functions merged into the overall weighted cost function "compare the actual deviations of a plan from the ideal CDVH with the maximum deviations allowed by the dose prescription." (Viggars at 422, 423 (Fig. 4); Ex. 1002 ¶108.) The score function that quantifies the deviation between a CDVH for a beam arrangement and the ideal CDVH for each of the target (overdose and underdose), organs-at-risk (overdose), or tissue (overdose) is determined by the following function in Viggars:

$$S_i = 10[1 - r_i]$$

(*Id.* at 423.)

In Viggars' segmented score function, the value "10 [is] for an ideal distribution, zero at the limit of acceptability, and negative when the dose-volume limit is violated." (*Id.*) The value "r_i" is the measure of the plan's deviation from the ideal dose prescription CDVH. (Ex. 1002 ¶109.) While a change in sign would

be used to incorporate the segmented score functions of Viggars within an overall cost function for *minimization* by Oldham's fast simulated annealing algorithm, such a change would be trivial and readily apparent to a person of ordinary skill in the art. (Ex. 1002 ¶111.) A representation of the overall cost function of Viggars to determine an optimal treatment plan using Oldham's segmented-cost method can be depicted as follows:

$$C_{TOTAL}(n) = WEIGHT_{PTV} \times -S_{target} + \sum_{j=1}^{m} (WEIGHT_{OAR_j} \times -S_{OAR,j}) + WEIGHT_{BODY} \times -S_{BODY}$$

(Ex. 1002 ¶113.)

Furthermore, the identification of weights would be further simplified for treatment plans that involve only a single organ-at-risk. (Ex. 1002 ¶94.) In such cases, a POSA would need only determine three suitable weighting factors—one for each of the target, organ-at-risk, and body tissue segmented costs. (Ex. 1002 ¶114.) Determining the three suitable weighting factors to achieve a clinical objective could easily be arrived at using the straightforward trial-and-error approach taught by Oldham and guided by the clinician's judgment concerning the relative importance

of applying the appropriate dose to the target versus the dose tolerated by the organ-at-risk or body tissue. (*Id.*)

Accordingly, Viggars overall cost function for optimization within Oldham's iterative optimization satisfies "incorporating a cost function at each iteration to approach correspondence of a CDVH associated with the proposed radiation beam arrangement to a CDVH associated with a predetermined desired dose prescription." (Ex. 1002 ¶115.) The combination of Oldham and Viggars therefore teaches this limitation.

5. "comparing the dose distribution to a prescribed dose for the tumor volume and surrounding tissue structures, and" (1[d])

Viggars teaches "objective score functions which quantify the deviation of the dose distribution from the dose prescription." (Viggars at 420.) As discussed above, the combination of Oldham and Viggars teaches replacing each segmented component of the cost function of Oldham with the corresponding CDVH-based score function of Viggars to yield an overall cost function. (Ex. 1002 ¶116.) The overall cost function to determine an optimal plan in Viggars "provide[s] a quantitative measure of how well a proposed treatment plan conforms to the dose prescription," and thus compares the dose distribution to a prescribed dose for the tumor volume and surrounding tissue structures." (*Id*. at 422.) Further, Viggars also teaches judging the quality of a proposed plan using "a visual display of the

prescribed dose-volume limits on the CDVH," and using "histograms of regret in either cumulative or differential form, which provide a striking and easily assimilated visual comparison of the CDVH or DDVH with the dose prescription," which also reflects a comparison between the dose distributions and prescribed doses for the tumor and surround tissue structures. (*Id*. at 420, 422 (Fig 3); Ex. 1002 ¶116.) Viggars also teaches the use of "other means of displaying the dose distribution such as isodose charts and images of regret" (*id.* at 419), which provides another way of comparing dose distributions with a dose prescription. (Ex. 1002 ¶116.) Therefore, Viggars and the combination of Oldham and Viggars teach this limitation.

6. "increasing or decreasing radiation beam intensity if the change of the proposed beam arrangement leads to a greater correspondence to the desired dose prescription to obtain an optimized radiation beam arrangement." (1[e])

Oldham teaches "increasing or decreasing the radiation beam intensity": "at each iteration all beam-weights are independently perturbed by adding a 'grain' of beam-weight" and "[t]he grains are randomly positive or negative and hence individual beam-weights can independently increase or decrease." (Oldham at 249; Ex. 1002 ¶117.) Oldham further discloses that an increase or decrease in beam intensity associated with the change in beam-weight would be accepted or rejected if it provides greater or lesser correspondence to the desired dose prescription numerically quantified by the cost function:

> A cost function is evaluated for the current beam-weight set and compared to the running cost-function value (i.e., the lowest cost-function value found from previous iterations). If the new cost function is lower than the running value, then the running value is set equal to the new value and the new beam-weight set is stored. If the new cost-function value is greater than the running value then no change is made to the running value and the algorithm moves to the next iteration.

(Oldham at 249.) As a result, "the algorithm finds beam-weight sets that successively converge to that set which corresponds to the minimum of the cost function." (*Id*.) The '096 patent uses "beam weight" and "intensity" synonymously, by describing in connection with Fig. 6A that "if 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." (Ex. 1001 at 5:28-30 (emphasis added).) Thus, Oldham teaches this limitation. (Ex. 1002 ¶118.)

XII. GROUND 2: CLAIM 18 IS OBVIOUS OVER OLDHAM IN VIEW OF VIGGARS AND MORRILL-1991

A. Prior Art and Date Qualification

Each limitation of claim 18, which is dependent on Claim, is disclosed or suggested by the combination of Oldham, Viggars, and Morrill-1991 *et al.*, *Treatment planning optimization using constrained simulated annealing*, Phys. Med. Biol. (36) No. 10, 1341-1361. (1991) (Ex. 1007) **("Morrill-1991")**.

Morrill-1991 is § 102(b) prior art, as established by a library date stamp. (Ex. 1003 ¶¶48-53.) Morrill-1991 is also over 20 years old therefore qualifying as ancient documents and was published in a well-known, reputable scientific journal. (Ex. 1002 ¶120.) None of Oldham, Viggars, and Morrill-1991 were before the Examiner during prosecution.

B. Brief Description of Morrill-1991 [Ex. 1022]

Morrill-1991 discloses "[a] variation of simulated annealing optimization called 'constrained simulated annealing'" that is used to "optimize beam weights and angles in radiation therapy treatment planning." (Morrill-1991 at 1341 (Abstract).) Morrill-1991 discloses the general features common to simulated annealing algorithms, but further explains that "[c]onstrained simulated annealing introduces the restriction that every sample configuration must satisfy a second set of additional predetermined constraints." (*Id.* at 1343.) "If the sample configuration fails to satisfy these additional constraints, it is rejected outright." (*Id.*) "Constrained simulated annealing is useful in those applications where some set of constraints must always be met, not just optimized." (*Id.*) "Although this second set of constraints can be characterized within the regular simulated annealing formalism by increasing the cost penalty for violating these constraints, it is computationally more efficient to separate them into a separate set." (*Id.*)

Morrill-1991 teaches two objective functions that use "dose-volume information." (*Id*. at 1344.) One of the objective functions, the "maximize dose with dose-volume limits (MDVL)," "maximizes the dose to isocentre, subject to target volume dose heterogeneity limits as well as maximum dose and dose-volume limits on the normal organs." (*Id*. at 1345.) "Table 2 shows the organ dose-volume constraints prescribed by the clinician for use with the MDVL cost function," as follows:

Table 2. Dose-volume constraints for the normal organs used by the MDVL objective function in the optimization of a treatment plan for a pancreatic tumour. The constraints are given as a maximum dose to the organ and a maximum volume to receive less than a given volume dose. Notice that the left kidney (distal to the tumour) has been given more restrictive dose constraints.

Organ	Maximum dose (Gy) (100% volume)	Maximum volume (%)	Volume dose (Gy)
External	63	75	45
Vertebral body	60	50	45
Spinal cord	45	50	40
Bowel	60	75	45
Liver	60	80	30
Left kidney	18	100	18
Right kidney	30	75	18

(*Id*. at 1347 (Table 2).)

C. Motivation to Combine and Reasonable Expectation of Success

Oldham, Morrill-1991 and Viggars are in the same field and they are each directed to using computer-implemented algorithms with cost (or "score") functions to quantitatively identify preferred beam arrangements for conformal radiotherapy. (Ex. 1002 ¶124.) For the same reasons as stated in Ground 1, one of skill in the art

would have been motivated to replace the cost function of Oldham with the cost function of Viggars with a reasonable expectation of success. (*Id.*)

A POSA would have been motivated to further combine the dose-volume constraints of Morrill-1991's constrained simulated annealing method with the optimization algorithm of Oldham and the cost function of Viggars. (Ex. 1002 ¶125.) Both Oldham and Morrill-1991 use simulated annealing algorithm and cost functions for the optimization of beam arrangement for conformal radiotherapy. (*Id.*) Morrill-1991 notes that "[p]erhaps the principal advantage of this technique [constrained simulated annealing] is its flexibility" since "[d]ifferent objective functions, constraints and annealing schedules are straightforward to implement." (Morrill-1991 at 1358.) "[T]he flexibility to specify individual organ dose-volume limits (especially to the spinal cord and kidneys) which implement the clinician's personal treatment methodology" is another advantage of Morrill-1991's constrained simulating technique. (*Id.* at 1354; Ex. 1002 ¶125.) A POSA would further understand that "[c]onstrained simulated annealing is useful in those applications where certain limitations must be met, not just optimized." (Morrill-1990 at 137.) Additionally, the use of constraints as opposed to merely changing the weighted penalties in a cost function "is computationally more efficient." (Morrill-1991 at 1343; Ex. 1002 ¶126.) These advantages, as well as the ability to place strict limits on maximum doses not to be violated by a treatment plan

in accordance with a dose prescription, would have motivated the combination of Morrill-1991's dose-volume constraints with Oldham and Viggars. (*Id.*)

A POSA would have reasonably expected to successfully use Morrill-1991's constrained simulated annealing approach with Oldham's fast simulated annealing algorithm and Viggars CDVH-based cost function. (Ex. 1002 ¶127.) A POSA would have recognized that compliance with such constraints would merely require a step within the SARP algorithm that checks whether the constraints are satisfied with every sample beam arrangement configuration at each iteration of the simulated annealing algorithm. (*See* Ex. Morrill-1990 at 139 (Fig. 1); Morrill-1991 at 1343; Ex. 1002 ¶128.) "Different objective functions, constraints and annealing schedules are straightforward to implement… If the objective function and dose constraints can be described by some type of quantitative algorithm, then they can be implemented using constrained simulated annealing." (Morrill-1991 at 1358.) A POSA would have known that these "[d]ifferent objective functions, constraints, and annealing schedules ***are very easy to implement***" in Morrill-1991's constrained simulated annealing approach to treatment plan optimization. (*See* Morrill-1990 at 137 (emphasis added); Ex. 1002 ¶128.)

Accordingly, one of skill in the art would have been motivated to replace the cost function of Oldham with the cost function of Viggars incorporating CDVH

subject to the dose-volume constraints of Morrill-1991 with a reasonable expectation of success. (Ex. 1002 ¶129.)

D. Claim 18: "The method of claim 1, 2, or 14 further comprising the step of allowing a radiation limit on the tissue structure to be exceeded by a set amount if such excess allows better conformation to the desired target CDVH curve."

As stated in Ground 1, a POSA would have been motivated and have a reasonable expectation of success in combining the fast simulated annealing algorithm of Oldham with the cost function of Viggars that "compare[s] the actual deviations of a plan from the ideal CDVH" to satisfy all elements of independent claim 1. (Ex. 1002 ¶130.) The maximum dose constraints placed on the treatment plan within the constrained variation of simulated annealing taught by Morrill-1991 satisfies the additional element provided by claim 18. (*Id.*)

With respect to the dose prescription, the '096 patent explains:

> The ***structure dosage limit*** value Bd′ is the desired dosage limit not to be exceeded in the volume of a sensitive structure; the structure maximum dosage value C′ is the maximum dose to be received by any portion of the structure; . . . and the portion of the structure volume which can have a dose greater than the goal dosage may be represented by structure percent over limit value Bv′.

(Ex. 1001 at 7:47-56 (emphasis added).)

Morrill-1991 used a dose prescription that provides radiation dose limits and maximum dose for the normal organs (i.e., "structures") in the same way as the '096 patent:

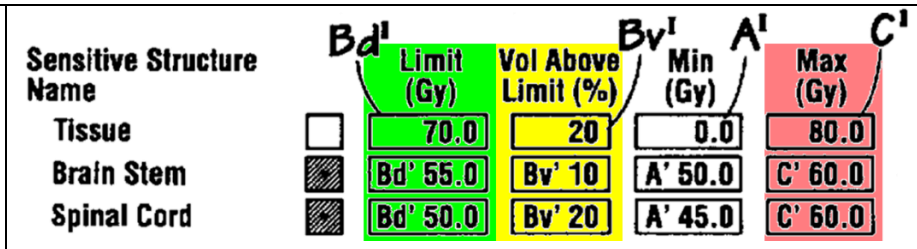
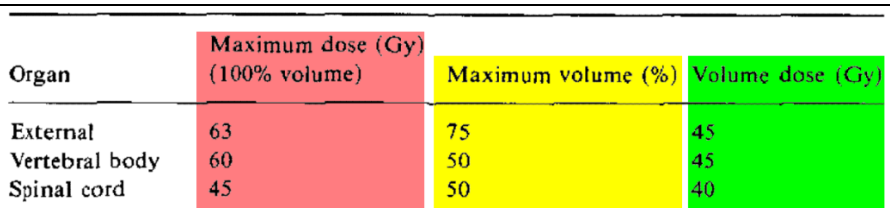
<table>
<tr><td>'096 patent, Fig. 5</td><td> 
</td></tr>
<tr><td>Morrill-1991,

Table 2</td><td> 
</td></tr>
</table>

(Ex. 1002 ¶132.) That is, Morrill-1991's "Volume dose" is the "structure dosage limit value Bd'" of the '096 patent and Morrill-1991's "Maximum dose" is a constraint on the maximum dose to the organ. (*Id.*)

Accordingly, the dose-volume constraints used by Morrill-1991's constrained simulated annealing method satisfies the limitation of claim 18. (Ex. 1002 ¶133.) For example, Table 2 of Morrill-1991 indicates that the spinal cord has a maximum dose of 45 Gy, a maximum volume of 50%, and a volume dose of 40 Gy. (*Id.*) This means that the dose to the spinal cord is subject to a radiation limit of 40 Gy, but up to 50% of the spinal cord volume can exceed this radiation limit by a set amount of 5 Gy to the maximum dose of 45 Gy. (*Id.*) Permitting the dose limit of a normal

organ to be exceeded by a set amount (i.e., up to the maximum dose) results in a "tradeoff" between conformation to the target and structure CDVH curves that favors conformation of the target CDVH over the structure radiation limit. (*Id.*) That is, by allowing the radiation limit on the normal organ to be exceeded, a plan that better conforms to the target CDVH at the expense of excess radiation to the normal organs up to a set amount defined by the maximum dose constraint can be created. (*Id.*)

If the Board concludes that Morrill-1991's constraints do not satisfy the limitation of claim 18, then the limitation would have been obvious in light of Morrill-1991's teachings. (Ex. 1002 ¶134.) Morrill-1991 teaches that where "the dose constraints are too restrictive," "the treatment planner may be required to relax the dose constraints and rerun the optimization." (Morrill-1991 at 1358.) Morrill-1991 explains that "[s]everal iterations of this dose constraint specification-optimization cycle may be required to finally produce a solution." (*Id.*) Accordingly, Morrill-1991 suggests modifying the "set amount" by which a radiation dose limit on normal organs may be exceeded in order to obtain a plan that provides an optimal beam arrangement that trades off additional dose to the normal organs with better conformation to the desired target CDVH, which satisfies claim 18. (Ex. 1002 ¶134.)

Claim 18 is therefore obvious over the combination of Oldham, Morrill-1991, and Viggars. (Ex. 1002 ¶135.)

XIII. GROUND 3: CLAIMS 1 AND 18 ARE OBVIOUS OVER CAROL-2 IN VIEW OF CAROL-17

A. Prior Art and Date Qualification

Each limitation of claim 1 is disclosed or suggested by the combination of Carol, *Chapter 2 – IMRT: Where we are today*, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 17-36 (Ex. 1020) **("Carol-2")** and Carol, *Chapter 17 – Where we go from here: one person's vision* The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 243-252 (Ex. 1021) **("Carol-17")**.

Both Carol-2 and Carol-17 are prior art under § 102(b) because they were publicly available more than one year before the provisional filing date of May 27, 1998. As of at least February 12, 1997, the Nomos Corporation website indicated that "The 'IMRT' Book" containing Carol-2 and Carol-17 "is available now." (Ex. 1004 (Butler Decl.) Ex. A at Page 0008.) On information and belief, BMI is a successor-in-interest to Nomos Corporation and the indication of the public availability of "the IMRT Book" as of February 12, 1997 is therefore a statement of a party opponent under Fed. R. Evid. 801(d)(2) that concedes the fact of the book's availability as prior art.

Additionally, the publisher's website indicated that the book containing Carol-2 and Carol-17 was also publicly available for purchase as of at least April 12,

1997. (Ex. 1004 (Butler Decl.) Ex. A at Page 0019.) Moreover, the book bears a copyright date of 1997 and therefore qualifies as an ancient document, which, at a minimum, demonstrates the prior art status of Carol-2 and Carol-17 at least under § 102(a) and this is further supported by a May 15, 1998 date-stamped copy of the book. (Ex. 1003 ¶¶60-64.)

Neither Carol-2 nor Carol-17 was before the Examiner during prosecution.

B. Brief Description of Carol-2 [Ex. 1020]

Carol-2 describes various aspects of the planning and implementation of IMRT plans, as well as specific details regarding the "PEACOCK intensity modulated radiation therapy (IMRT) system." (*See* Carol-2 at 17.) "PEACOCK Plan uses an interface which involves assigning graded weights and priorities to the structures and targets in order to achieve desired results." (Carol-2 at 21.) Carol-2 explains that reverse IMRT treatment planning is:

> [E]xemplified by simulated annealing which, as applied to radiation therapy treatment planning, proceeds by randomly changing beam weights, then evaluating the effect of each change on the dose distribution. The acceptability of a change is determined by a cost function which is a mathematical quantification of how conflicting goals will be resolved; a higher cost is produced when the resulting dose distribution strays from the desired dose distribution. In general,

> although not always, the production of a higher cost results in the throwing out the change in beam weight . . . The iterative changing of beam weights continues until the cost reaches a user-designated acceptable level."

(Carol-2 at 20-21.)

C. Brief Description of Carol-17 [Ex. 1021]

Carol-17 describes certain state of the art features of IMRT and identifies additional technological advancements within the field. (Carol-17 at 243-244.) Carol-17 teaches the "user interfaces are changing in order to provide a more 'clinically relevant' and 'experience friendly' way of entering desired dose information." (Carol-17 at 247.) Carol-17 explains that "a user-interface has been created for one such inverse planning system, CORVUS," which "uses partial volume information for each structure out of which CDVH curves are generated and used as the goal by the optimizer." (*Id.*)

D. Motivation to Combine and Reasonable Expectation of Success

Both Carol-2 and Carol-17 are in the same field of intensity modulated radiotherapy treatment (IMRT) and planning, and included within the same IMRT book. A POSA would have been motivated to combine the CORVUS program's CDVH-based cost function of Carol-17 with the simulated annealing PEACOCK program disclosed in Carol-2 to obtain an optimized treatment plan that has the goal

of optimizing to the desired CDVHs of the dose prescription. (Ex. 1002 ¶141.) The motivation in doing so is expressly disclosed in the references themselves and would also provide benefits that would have been readily apparent to a POSA. (*Id.*)

A POSA would have been motivated to use the CDVH-based cost function disclosed in Carol-17 because Carol-17 expressly discloses that the CORVUS user interface would "provide a more 'clinically relevant' and 'experience friendly' way of entering desired dose information." (Carol-17 at 247; Ex. 1002 ¶142.) One of ordinary skill would have been further motivated because of the expressly stated understanding that "[c]linicians have begun to learn to 'think' in terms of partial volumes" and "[i]t therefore seems natural to expect that the definition of what the desired result should look like will be made in a similar manner using partial volumes." (*Id.*) That is, a POSA would recognize the benefit of using the CDVH-based cost function of Carol-17 to optimize a treatment plan within the simulated annealing approach of Carol-2 in order to computationally perform the same type of CDVH-based evaluation of treatment plans that were long used by clinicians to evaluate rival treatment plans. (Ex. 1002 ¶142.) Specifically, this would allow the computer optimization to make a cost-function-based assessment of "how well does the actual result compare to the desired result[s]," and thereby allow the computer to test a large number of beam arrangements as part of achieving a SARP optimized

plan that achieves a clinician's desired partial volume dose prescription. (Carol-17 at 247; Ex. 1002 ¶142.)

A POSA would have reasonably expected success in using the CDVH-based cost function of Carol-17 for CORVUS with the SARP optimization technique taught by Carol-2 for the PEACOCK Plan program. (Ex. 1002 ¶143.) Carol-17 explains that "CORVUS uses a unique Area Cost Function (ACF) which is explicit in its resolution of conflicts" and that "[a]fter a CDVH is constructed from user-entered partial volume values, the system divides the CDVH into regions and automatically assigns a relative weight to each." (Carol-17 at 247.) Carol-17 explains that "[t]he default weights favor structures over targets when such conflicts exist; all structure limits, no matter how severe, will be met before target goals are met." (*Id.*) "The user has the option of selecting, on a target-by-target basis, whether target goals or structure limits will prevail." (*Id.*)

Accordingly, a POSA would have been motivated to implement the Area Cost Function (ACF) of Carol-17 for each of the target(s) and structure(s) to obtain an overall cost function for optimization by the SARP algorithm taught by Carol-2 with a reasonable expectation of success. (Ex. 1002 ¶144.)

E. Claim 1

All elements of claim 1 are satisfied by incorporating the CDVH-based cost function disclosed in Carol-17 that "uses partial volume information for each

structure out of which CDVH curves are generated an used as the goal by the optimizer" within the simulated annealing optimization methods disclosed by Carol-2. (Ex. 1002 ¶145.) Claim 1 is therefore obvious over Carol-2 and Carol-17.

1. "A method of determining an optimized radiation beam arrangement for applying radiation to a tumor target volume while minimizing radiation of a structure volume in a patient, comprising the steps of:" (Preamble)

To the extent the preamble is limiting, it is disclosed by Carol-2 and Carol-17. (Ex. 1002 ¶146.) Carol-2 discloses "the PEACOCK intensity modulated radiation therapy (IMRT) system." (Carol-2 at 17.) Specifically, Carol-2 teaches that when IMRT methods are used "a relatively uniform dose can be achieved in the target while avoiding the deposition of high dose to surrounding structures" and is able "to minimize dose to regions of risk while maximizing dose and dose homogeneity to the target volume within the constraints of the delivery devices available." (*Id*. at 18, 20.) Thus, Carol-2 teaches this limitation.

Carol-2's relevant disclosures of the preamble would not be altered by incorporating the CDVH-based cost function of Carol-17 (CORVUS) with Carol-2's simulated annealing optimization algorithm (PEACOCK). (Ex. 1002 ¶147.) As Carol-17 teaches, the optimized IMRT treatment plan "will deliver a specified dose of radiation shaped to correspond to the target volume while limiting the dose delivered to sensitive volumes which may surround the target volume. (Carol-17 at

248; Ex. 1002 ¶147.) Accordingly, Carol-17 also discloses the preamble of claim 1. (Ex. 1002 ¶147.)

2. "using a computer to computationally obtain a proposed radiation beam arrangement;" (1[a])

Carol-2 describes "treatment planning for IMRT," which is "usually a computer-based inverse operation." (Carol-2 at 20.) The planning program generates "the beams and beam weights needed to achieve user defined goals." (*Id*.) The SARP algorithm taught by Carol-2 "proceeds by randomly changing beam weights, then evaluating the effect of each change on the dose distribution." (*Id*.) Accordingly, Carol-2's disclosure of a computer-implemented simulated annealing algorithm satisfies the claimed function of computationally obtaining a proposed radiation beam arrangement by proposing new beam weights at each iteration of the optimization process. (Ex. 1002 ¶148.) The corresponding structure is satisfied by Carol-2 because the simulated annealing disclosed therein is a SARP algorithm and the proposed beam weights are used as input for subsequent optimization. (*Id*.) Accordingly, claim element 1[a] is disclosed by Carol-2.

If the Board concludes that the computer-implemented function of claim element 1[a] is not drafted in means-plus-function format, Carol-2's disclosed use of a computer to propose new beam weights at each iteration, as identified above, satisfies the claim limitation. (*Id.* ¶149.)

3. "using a computer to computationally change the proposed radiation beam arrangement iteratively," (1[b])

The computer used in Carol-2 discloses an iterative simulated annealing algorithm that "proceeds by randomly changing beam weights, then evaluating the effect of each change on the dose distribution." (Carol-2 at 20.) "The acceptability of a change is determined by a cost function which is a mathematical quantification of how conflicting goals will be resolved," and "[t]he iterative changing of beam weights continues until the cost reaches a user-designated acceptable level." (*Id*. at 20-21.) Therefore, Carol-2 discloses this claim element, including both the claimed computer-implemented function and corresponding structure in the form of the computer programmed with the disclosed SARP algorithm that randomly changes the beam weights at each iteration. (Ex. 1002 ¶150.) If the Board concludes that the computer-implemented function of claim element 1[b] is not drafted in means-plus-function format, Carol-2's disclosed use of a computer to change the beam weights at each iteration, as identified above, satisfies the claim limitation. (Ex. 1002 ¶151.)

4. "incorporating a cost function at each iteration to approach correspondence of a CDVH associated with the proposed radiation beam arrangement to a CDVH associated with a predetermined desired dose prescription;" (1[c])

Carol-2 teaches a simulated annealing algorithm using a cost-function, which is "a mathematical quantification of how conflicting goals will be resolved" and "a mathematical statement of what is considered a good result." (Carol-2 at 20-21.)

"The iterative changing of beam weights continues until the cost reaches a user-designated acceptable level." (*Id*. at 21.) "PEACOCK Plan uses an interface which involves assigning graded weights and priorities to the structures and targets in order to achieve the desired result" and "[t]he overall calculated cost is based on the weight assigned to each structure and target." (*Id*.)

It would have been obvious to a POSA to incorporate a cost function of approaching correspondence of a CDVH into the cost function in Carol-2. (Ex. 1002 ¶153.) However, to the extent Patent Owner argues that Carol-2 does not teach or suggest this claim limitation, it is expressly taught and suggested by Carol-17.

Carol-17 discloses an inverse planning system, CORVUS, which "uses partial volume information for each structure out of which ***CDVH curves are generated and used as the goal by the optimizer***." (Carol-17 at 247 (emphasis added).) Carol-17 further discloses:

> For each target, the user enters: goal, minimum dose, maximum dose and percent volume which is allowed to be underdosed. For each structure, the user enters: desired limit, minimum dose, maximum dose and percent volume which can be greater than limit. The system creates CDVH curves for the targets and structures from these entries which are used by the optimizer as a representation of the desired dose distribution.

(Carol-17 at 247.) "After a CDVH is constructed from user-entered partial volume values, the system divides the CDVH into regions and automatically assigns a relative weight to each," which are "used to resolve conflicts between the various CDVH regions defined by the target goals and structure limits." (*Id.*)

Thus, the cost function taught by Carol-17 is used to optimize the CDVH for iteratively proposed beam arrangements to approach correspondence of a CDVH associated with the pre-determined desired dose prescription. It would have been obvious to a POSA to incorporate the cost function of Carol-17 in the iterative simulated annealing algorithm disclosed by Carol-2. (Ex. 1002 ¶155.) Accordingly, the combination of Carol-17 and Carol-2 also satisfies this limitation.

5. "comparing the dose distribution to a prescribed dose for the tumor volume and surrounding tissue structures, and" (1[d])

Carol-17 teaches that "[t]he system creates CDVH curves for the targets and structures . . . which are used by the optimizer as a representation of the desired dose distribution." (Carol-17 at 247.) Carol-17 further teaches that a weighted comparison between the proposed CDVH curves (i.e., the proposed dose distribution) against the desired CDVH curves (i.e., the prescribed dose distribution) is "used to resolve conflicts between the various CDVH regions defined by the target goals and structure limits." (*Id.*) Accordingly, use of the cost function taught by Carol-17 performs the step recited in claim element 1[d]. (Ex. 1002 ¶156.)

Carol-17 further teaches that "a SCORE function . . . can be applied to assess how well an achieved plan compares to the desired result for a given target or structure." (Carol-17 at 247-248.) The SCORE function of Carol-17 compares "how well the actual DVH for the structure/target fits the desired DVH." (*Id.* at 248.) Thus, Carol-17's SCORE function also satisfies this limitation. (Ex. 1002 ¶157.)

6. "increasing or decreasing radiation beam intensity if the change of the proposed beam arrangement leads to a greater correspondence to the desired dose prescription to obtain an optimized radiation beam arrangement." (1[e])

Carol-2 teaches a standard SARP method in which random changes are made iteratively to the beam weights, that "[t]he acceptability of a change is determined by a cost function," and that "a higher cost is produced when the resulting dose distribution strays from the desired dose distribution." (Carol-2 at 20.) Carol-2 further teaches that "[i]n general, although not always, the production of a higher cost results in the throwing out of the change in beam weight" and that "[t]he iterative changing of beam weights continues until the cost reaches a user-designated acceptable level." (*Id*. at 20-21.) Carol-2 further teaches that in IMRT "the intensity of the beam is varied across the treatment field" and that "[a]t its most basic level, all radiation therapy treatment planning can be viewed as involving the delivery of

intensity modulated fields." (*Id.* at 18-19.) Thus, a POSA understands that Carol-2 teaches this limitation or renders it obvious. (Ex. 1002 ¶158.)

F. Claim 18: "The method of claim 1, 2, or 14 further comprising the step of allowing a radiation limit on the tissue structure to be exceeded by a set amount if such excess allows better conformation to the desired target CDVH curve."

Claim 18 is obvious over the combination of Carol-2 and Carol-17. (Ex. 1002 ¶159.) Carol-17 teaches that "weights are used to resolve conflicts between the various CDVH regions defined by the target goals and structure limits;" "[t]he default weights favor structures over targets when such conflicts exist; all structure limits, no matter how severe, will be met before target goals are met;" and "[t]he user has the option of selecting, on a target-by-target basis, whether target goals or structure limits will prevail." (Carol-17 at 247.) When the user sets the weights to favor targets over structures, the "target goals" prevail over the "structure limits" and the step of claim 18 is satisfied. (Ex. 1002 ¶159.)

XIV. GROUND 4: CLAIM 18 IS OBVIOUS OVER CAROL-2 IN VIEW OF CAROL-17 AND MORRILL-1991

To the extent Patent Owner argues that claim 18 is not disclosed by the combination of Carol-2 and Carol-17 of Ground 3, it is taught and/or suggested by Morrill-1991. (Ex. 1002 ¶160.) The prior art status and relevant disclosures of these references are provided above in Ground 3 (Carol-2 and Carol-17) and Ground 2 (Morrill-1991).

A. Motivation to Combine and Reasonable Expectation of Success

As described in Ground 2, Morrill-1991 discloses the use of dose constraints (i.e., maximum dosages) on normal organs. A person of ordinary skill in the art would have been motivated to incorporate the constrained simulated annealing approach of Morrill-1991 into the simulated annealing methodology Carol-2 with the CDVH-based cost functions of Carol-17 with a reasonable expectation of success for the same reasons outlined in Ground 2 with respect to the combination of Oldham and Viggars. (Ex. 1002 ¶161.) That is, for example, a POSA would have been motivated to include Morrill-1991's constraints to provide strict limits on how much a given dosage limit for normal organs could be exceeded during optimization because doing so "is useful in those applications where certain limitations must be met, not just optimized" and because it "is computationally more efficient." (Morrill-1990 at 137; Morrill-1991 at 1343.)

A POSA would have reasonably expected to successfully use Morrill-1991's variation of simulated annealing with the disclosures of Carol-2's simulated annealing methodology using the CDVH-based cost function of Carol-17 for the same reasons as set forth in Ground 2. (Ex. 1002 ¶162.) For example, Morrill-1991 expressly discloses that "[d]ifferent objective functions, constraints and annealing schedules are straightforward to implement." (Morrill-1991 at 1358; Ex. 1002 ¶162.) A POSA would have known that these "[d]ifferent objective functions,

constraints, and annealing schedules ***are very easy to implement***." (*See* Morrill-1990 at 137 (emphasis added); Ex. 1002 ¶162.)

B. Claim 18: "The method of claim 1, 2, or 14 further comprising the step of allowing a radiation limit on the tissue structure to be exceeded by a set amount if such excess allows better conformation to the desired target CDVH curve."

The step of claim 18 is satisfied and rendered obvious by the maximum radiation dose constraints placed on normal organs by the prescription constraints taught by Morrill-1991, as described in Ground 2 above, in combination with Carol-2 and Carol-17. (Ex. 1002 ¶163.) There is nothing about the simulated annealing taught by Carol-2 or the CDVH-based cost functions of Carol-17 that would pose any material difference in the use of Morrill-1991's constraints to satisfy the step of claim 18 as described with the simulated annealing method of Oldham in Ground 2. (*Id.*) Specifically, Morrill-1991's normal organ constraints would allow the dosage limit on a normal organ to be exceeded by a set amount up to the maximum dose during optimization, which would result in a plan that better conforms to the target CDVH at the expense of the excess radiation to the normal organs up to that maximum dose constraint. (*Id.*) Morrill-1991 also indicates that "the treatment planner may be required to relax the dose constraints and rerun the optimization" (Morrill-1991 at 1358), thereby teaching that it would have been obvious to change the set amount that a radiation limit can be exceeded during optimization in order to

obtain an optimal plan that better conforms to the desired target CDVH. (Ex. 1002 ¶163.)

XV. CONCLUSION

Petitioner respectfully requests institution of review of claims 1 and 18.

Dated: October 18, 2019

Respectfully submitted,

By: / *Heidi L. Keefe* /
Heidi L. Keefe
Reg. No. 40,673
Counsel for Petitioner

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 13,814 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 18, 2019

COOLEY LLP
ATTN: Patent Group
1299 Pennsylvania Ave. NW,
Suite 700
Washington, DC 20004
Tel: (650) 843-5001
Fax: (650) 849-7400

/ *Heidi L. Keefe* /
Heidi L. Keefe
Reg. No. 40,673

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. 6,393,096 B1,** including all exhibits (**Nos. 1001-1005, 1008-1030**) and related documents, are being served via Federal Express on the 18th 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 the PO 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 the PO in the litigation pending before the U.S. District Court for the District of Delaware entitled *Best Medical International, Inc. v. Varian Medical Systems Inc. and Varian Medical Systems International AG*, Case No. 1:18-cv-01599-UNA (D. Del.) as follows:

Geoffrey G. Grivner
BUCHANAN INGERSOLL & ROONEY PC
919 NORTH MARKET STREET
SUITE 1500
WILMINGTON, DE 19801

DATED: October 18, 2019

COOLEY LLP
ATTN: Patent Docketing
1299 Pennsylvania Avenue NW
Suite 700
Washington, D.C. 20004
Tel: (650) 843-5001
Fax: (650) 849-7400

/ *Heidi L. Keefe* /
Heidi L. Keefe
Reg. No. 40,673