UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELEKTA INC.,
Petitioner

v.

BEST MEDICAL INTERNATIONAL, INC.,
Patent Owner.

Case No.: IPR2020-00970

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

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

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LIST OF EXHIBITS

Exhibit	Description
1001	U.S. Patent No. 6,393,096 B1 ("the '096 patent")
1002	Expert Declaration of Dr. Kenneth Gall
1003	Expert Declaration of Hall-Ellis
1004	Declaration of Christopher Butler
1005	Notice of Allowance for U.S. Application 09/320,980 dated Sept. 1, 2000
1006	Peacock™: A System for Planning and Rotational Delivery of Intensity-Modulated Fields," *International Journal of Imaging Systems and Technology* (Spring 1995) ("Carol-1995")
1007	B. Curran, "Conformal Radiation Therapy Using a Multileaf Intensity Modulating Collimator" (1997) ("Curran-5")
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")
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 Systems 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")

Exhibit	Description
1016	Drzymala, R.E. et al., "Dose-Volume Histograms," *Int. J. Radiation Oncology Biol. Phys.*, 21:71-78 (1991) ("Drzymala 1991")
1017	U.S. Pat. No. 5,596,619
1018	S. Kirkpatrick, "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 prostate," *Radiology & Oncology* (1995) ("Oldham 1995")
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	*Reserved*
1023	Carol, M.P., "An automatic 3D Conformal Treatment Planning System for Linear Accelerator Based Beam Modulation Radiotherapy," *Proceedings of the XIth International Conference* (March 20-24, 1994)
1024	*Reserved*
1025	*Reserved*
1026	*Reserved*
1027	*Reserved*
1028	*Reserved*
1029	*Reserved*
1030	*Reserved*
1031	Morrill, S.M. et al., "Dose Volume considerations with linear programming optimization," *Phys. Med. Biol.*, 18(6) (Nov/Dec 1991) ("Morrill-1991")

Elekta Inc. ("Elekta" or "Petitioner") respectfully submits this petition for *Inter Partes* Review of claims 43, 44, and 46 of U.S. Patent No. 6,393,096 (Ex. 1001) ("the '096 patent"). The Board previously instituted review of these claims based on the petition filed by *Varian Medical Systems, Inc.* ("Varian") in IPR2020-00072. The challenges to claims 43, 44, and 46 presented herein are substantively identical to Varian's challenges in IPR2020-00072 and are based on the same evidence as presented in IPR2020-00072, as further explained in the motion for joinder submitted with this petition.

I. INTRODUCTION

The method claims of the '096 patent challenged in this petition are broad, open "comprising" claims that cover obvious features of a standard radiotherapy treatment planning workflow. Radiotherapy is the use of beams of radiation for treating tumors. Radiotherapy planning is the predetermined arrangement of beams (i.e., their number, orientations, and intensities) used to treat a tumor. The aim of treatment planning is to provide a sufficient cumulative dose of radiation to kill the tumor while minimizing the incident radiation exposure of the surrounding organs according to a doctor's radiation dose prescription.

By the May 27, 1998 presumptive priority date of the '096 patent, the relevant art in the field was well-established and littered with prior art references material to the patentability of claims 43, 44, and 46. The limited references provided by the

patentees during prosecution included only a sliver of the knowledge within the art. Critically, the patentees failed to disclose highly material prior art publications authored by inventors of the ’096 patent, which each expressly disclose, suggest, or render obvious to a person of ordinary skill the presently challenged claims. Each of the invalidity Grounds in this Petition rely primarily or entirely on the inventors’ own prior art publications.

During prosecution, the examiner allowed issuance of all claims of the ’096 patent as originally submitted without a single rejection. With respect to claims 43, 44, and 46, the Examiner’s relevant reason for allowance was based on the conclusion that “providing the user with a range of input values indicating the importance of the values or the objects being irradiated” is “neither shown nor fairly suggested in the prior art.” (Ex. 1005, Notice of Allowability.) But, in references not before the Examiner and published years before the priority date of the ’096 patent, the literal term “importance factor” was already coined and used within the art to numerically define the relative importance of different objects being irradiated (e.g., the tumor and sensitive structures surrounding the tumor).

In their prior art publications, the inventors eschewed literal description of an “importance factor” *per se* and instead recast the “importance factor” as an “aggressiveness” constraint and/or “weight(s).” For example, the Carol-1995 publication of Ground 1, teaches an “aggressiveness” constraint that “influences ***the***

relative importance of delivering the prescribed dose to the complete target versus sparing . . . sensitive structures (relative values '***WeightI***' and '***WeightJ***')." (Ex. 1006, Carol-1995 at 58 (emphasis added).) In a similar fashion, the Curan-5 publication of Grounds 2 and 3, teaches the use of parameters identified as "weights" that "determine ***the relative importance***" of the tumor target and the surrounding structures. (Ex. 1007, Curran-5 at 85.) Curran-5 also expressly teaches that "typical weights" are from "0.0" to "2.0." (*Id.*) As such, these disclosures directly contradict the Examiner's rationale for allowing issuance of the claims.

Since the Grounds presented herein demonstrate a reasonable likelihood that Petitioner would prevail in demonstrating that claims 43, 44, and 46 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 Parties-in-Interest Under 37 C.F.R. §42.8(b)(1)

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

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

Patent Owner asserted the '096 patent in *Best Medical International, Inc.* v.

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

The '096 patent was challenged in *Elekta Inc. v. Best Medical International, Inc.,* IPR2020-00074, filed October 18, 2019, for which institution was denied on May 1, 2020; and *Varian Medical Systems, Inc., v. Best Medical International, Inc.,* IPR2020-00072, filed October 18, 2019. Based upon the latter Varian Petition, the Board instituted review of claims 43, 44, and 46 on May 1, 2020.

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

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

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

D. Service Information

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

843-8777). Pursuant to 37 C.F.R. §42.8(b)(4), Petitioner consents to e-mail service at: tamara.fraizer@squirepb.com; sfripdocket@squirepb.com.

III. FEE PAYMENT

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

IV. REQUIREMENTS 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. Other than the petitions noted above, and *Varian Medical Systems, Inc., v. Best Medical International, Inc.,* IPR2020-00071, filed October 18, 2019, 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 43, 44, and 46 and requests that the Board find the claims unpatentable under 35 U.S.C. §103 (pre-AIA):

Ground	Claims	Basis of Invalidity
1	43, 44, and 46	Obvious over Carol-1995 (Ex. 1006) in view of Viggars (Ex. 1015)
2	43, 44, and 46	Obvious over Curran-5 (Ex. 1007) in view of Carol-2 (Ex. 1020)
3	43, 44, and 46	Obvious over Curran-5 (Ex. 1007) in view of Carol-17 (Ex. 1021)

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. ¶¶1-13.) Dr. Gall's declaration includes additional exhibits (Exs. 1001-1023) that provide further information regarding the relevant technology and the state of the prior art.

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

The Board should institute *inter partes* review of claims 43, 44, and 46 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. (Ex. 1008, Webb 1993 at ix.) The therapeutic 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 been known since the early 1900s 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. (Ex. 1009, Webb-1989 at 1349.) In this regard, "[i]t is well recognized that . . . normal tissue tolerance critically depends on the volume of irradiated tissue." (Ex. 1010, Lawrence-1990 at 1041; *see also* Ex. 1011, 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, e.g.*, Ex. 1012, Goitein-1992 at 247.)

B. Radiotherapy Instruments

The radiation beams used for radiotherapy are typically supplied by "high-energy computer-controlled linear accelerators." (Ex. 1013, Morrill-1990 at 135.) Such radiotherapy instruments have an adjustable patient table generally centered

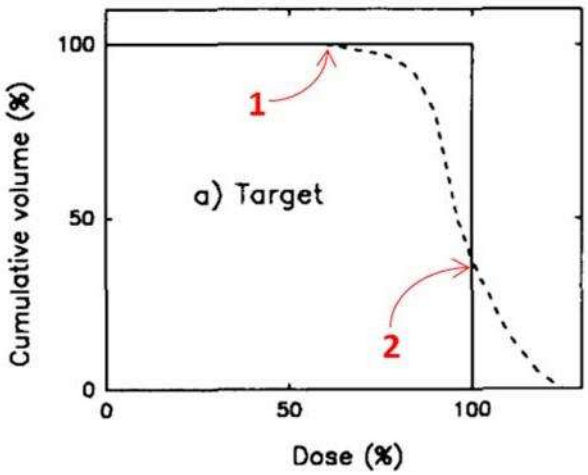
within the focus of a rotatable gantry containing a beam shaping device or "collimator" to apply beams with different trajectories, intensities, and shapes that conform to the two-dimensional "beams-eye" view of the tumor at each trajectory. (Ex. 1014, Webb-1995 at 71.) As such, "treatment accelerators 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, a process generally known as "conformal" radiotherapy. (Ex. 1009, 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. (Ex. 1015, Viggars 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.* at 419.) 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. (Ex. 1012, Goitein-1992 at 251-252.)

An ideal dose prescription would be "uniform at 100% of the prescribed dose [in the target] and zero in all other tissues." (Ex. 1015, 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. (Ex. 1010, Lawrence-1990 at 1041-42.)



(*See* Ex. 1015, 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. (Ex. 1012, 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." (Ex. 1012, Goitein-1992 at 251; Ex. 1016, Drzymala-1991 at 77 ("Their greatest strength is their ability to provide rapid screening of plans.").) "Their acceptance has been rapid and widespread." (Ex. 1012, Goitein-1992 at 251.) CDVHs are recognized as "an essential feature of a modern treatment planning system." (*Id.* at 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. (*See* Ex. 1016, Drzymala-1991 at 77.)

D. Radiotherapy Treatment Planning

The flexibility provided by radiotherapy instruments has been "accompanied by advances in radiation therapy treatment planning—[i.e.,] the process of selecting the proper patient position, radiation beams, and radiation doses required to treat the given patient." (Ex. 1013, 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." (Ex. 1011, 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). (Ex. 1009, 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.*; *see also, e.g.*, Ex. 1015, Viggars at 419.) This process can be referred to as *forward* treatment planning. (Ex. 1014, 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" that satisfy the prescription. (Ex. 1009, Webb-1989 at 1350.) That is, "[g]iven a prescription of desired outcomes, compute the best beam arrangement." (Ex. 1014, 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" (Ex. 1009, Webb-1989 at 1350) and requires that the optimization be "solved by a computer with human guidance rather than by human experience alone." (Ex. 1014, Webb-1995 at 71).

An illustrative overall workflow for use of a radiation planning system, which is identical to Fig. 2 in the '096 patent, is provided in Fig. 10 of U.S. Pat. No.

5,596,619 to Carol:

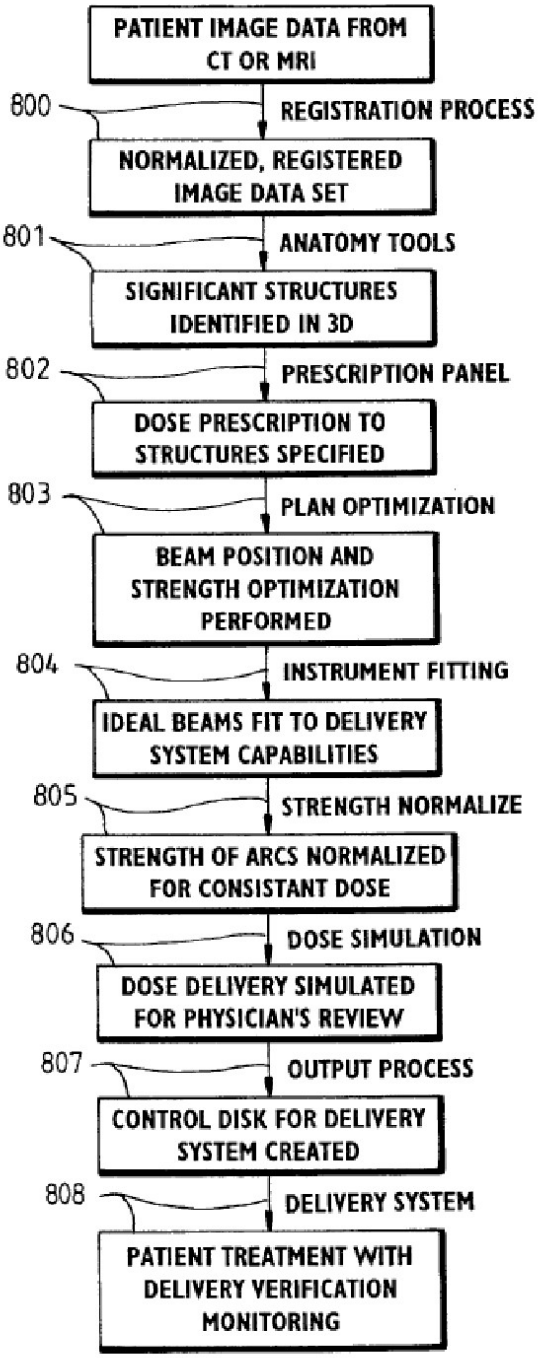


Fig. 10

Ex. 1017, U.S. 5,596,619 at Fig. 10; Ex. 1002 ¶42.)

As part of the Prescription step (802), the physician "input[s] into the planning

system the desired goal of the radiation therapy treatment, in terms of desired target dose, sensitive structure limits, delivery complexity, and aggressiveness," which are "utilized in the plan optimization step." (*Id.* at 17:1-9.) "Aggressiveness relates to the relative importance of maximally treating the target, or tumor, as compared with sparing sensitive adjacent anatomical structures." (*Id.*)

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. (Ex. 1014, Webb-1995 at 71-72.) The iterative optimization method of simulated annealing is one such method used to optimize inverse treatment plans, which has been referred to as simulated annealing radiotherapy planning (SARP). (Ex. 1009, Webb-1989 at 1350; *see also* Ex. 1014, Webb-1995 at 72.)

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." (Ex. 1009, Webb-1989 at 1352; *see also, e.g.*, Ex. 1018, Kirkpatrick-1983 at 671.) 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." (Ex. 1014, Webb-1995 at 72.) The function used by a simulated annealing method is referred to as an "objective" or "cost" function. (*E.g.*, Ex. 1009, Webb-1989 at

1358; Ex. 1018, Kirkpatrick-1983 at 671.)

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* Ex. 1009, Webb-1989 at 1349.) "The aim of optimization would be to minimize the cost function, possibly subject to constraints." (Ex. 1008, Webb-1993 at 344.) "The minimum of the cost function defines the theoretical ideal dose distribution (and beam-weight set) which the optimization algorithm attempts to achieve." (Ex. 1019, Oldham-1995 at 250.)

As such, 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. (Ex. 1013, Morrill-1990 at 136.) 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." (*Id.* at 135.)

Determining an "optimal" beam arrangement with SARP involves iteratively evaluating various beam arrangements to find one that minimizes a cost function that numerically quantifies compliance with the treatment objectives. (*See, e.g.*, Ex. 1014, Webb-1995 at 72; Ex. 1009, Webb-1989 at 1350 (the problem of the optimization method "becomes that of *determining* the optimum weights for the

beam elements at each orientation *given* the dose prescription" and "is solved by the method of simulated annealing").) That is, 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—within the cost function. (Ex. 1014, Webb-1995 at 78; Ex. 1019, Oldham-1995 at 250.)

VI. SUMMARY OF THE '096 PATENT

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

The '096 patent is entitled "Planning Method and Apparatus for Radiation Dosimetry." (Ex. 1001.) The '096 patent was filed on May 27, 1999, claims priority to provisional application No. 60/087,049 filed on May 27, 1998, and issued on May 21, 2002. (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 was well-known in the prior art: "[i]t is known that a vast majority of tumors can be eradicated completely if a sufficient radiation dose is delivered to the tumor volume; however, complications may result from use of the necessary effective radiation dose, due to damage to healthy tissue which surrounds the tumor, or to other healthy body organs located close to the tumor." (Ex. 1001 at 1:17-23.) 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 at 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.) "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 alleges to have disclosed "an improved optimized treatment planning system, which accounts for multiple treatment parameters for both a target and multiple surrounding structure types." (Ex. 1001 at 5:54-57.) The '096 patent 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 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: "***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 provided by the computer-implemented SARP algorithm, the '096 patent explains that the physician reviews the plan prior to "approv[ing] the radiation plan for patient delivery." (Ex. 1001 at 15:63-65.)

During prosecution, the examiner allowed all claims as originally submitted without rejection. (Ex. 1005, September 1, 2000 Notice of Allowability.) The reasons for allowance provided by the examiner included, with respect to the presently challenged claims, the following:

> [T]he claims address a method and apparatus of determining an optimized radiation beam arrangement for applying radiation to a tumor target . . . [by] providing the user with a range of input values indicating the importance of the values or the objects being irradiated. This feature is neither shown nor fairly suggested in the prior art.

(Ex. 1005, September 1, 2000 Notice of Allowability.)

VII. STATEMENTS OF MATERIAL FACT

The following statements of material fact are 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, all details of simulated annealing radiotherapy planning (SARP) techniques were known in the art and would have been within the knowledge of a POSA, as stated in the ’096 patent at 8:41-44.
2. U.S. Patent No. 5,596,619 (the ’619 patent) to Carol is prior art to the ’096 patent because it issued on January 21, 1997, more than one year before the May 27, 1998 provisional filing date for the ’096 patent.
3. The flow diagram of the radiation planning system in Fig. 10 of the prior art ’619 patent would have been within the knowledge of a POSA prior to the earliest priority date of the ’096 patent.

VIII. 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 ¶¶15-17.)

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.*)

For purposes of this Petition, and consistent with the Board's decision in IPR2020-00072 dated May 1, 2020, Petitioner does not believe that any claim terms require explicit construction from the Board at this time.

X. THE CLAIMS OF THE '096 PATENT HAVE A PRIORITY DATE OF NO EARLIER THAN MAY 27, 1998.

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 102(b) date of May 27, 1997 and the 102(a) provisional filing date of May 27, 1998.

XI. GROUND 1: CLAIMS 43, 44, AND 46 ARE OBVIOUS OVER CAROL-1995 IN VIEW OF VIGGARS

A. Prior Art and Date Qualification

Each limitation of claims 43, 44, and 46 is disclosed, suggested, or obvious by the combination of Carol *et al.*, *PeacockTM: A System for Planning and Rotational Delivery of Intensity-Modulated Fields*, Int. J. Imaging Systems & Tech., Vol. 6, 5661 (1995) (Ex. 1006,) **("Carol-1995")** 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) (Ex. 1015) **("Viggars")**.

Carol-1995 and Viggars are prior art under §102(b) because they were published more than one year before May 27, 1998, the provisional filing date of the '096 patent. Neither Carol-1995 nor Viggars was before the examiner during prosecution.

B. Brief Description of Carol-1995

Carol-1995 discloses the "Peacock" system for treatment planning and delivery. (Ex. 1006, Carol-1995 at 56 ("The Peacock three-Dimensional Conformal System plans and implements . . . conformal treatment plans.").) Carol-1995

describes the Peacock system as using an approach where "[t]he parameters driving beam modulation and field shaping are generated by a three-dimensional planning computer using a simulated annealing algorithm guided by cost functions which quantify prescribed treatment constraints." (*Id*.)

"Peacock defines cost as the sum of weighted costs for each structure and target (weights as specified during 'Prescription')." (*Id.* at 57.) "The relative values of "WeightI" (target weight) and "WeightJ" (structure weights) emphasize or deemphasize the contribution of each target and structure to the total cost." (*Id.* at 58.) Carol-1995 teaches that "[t]he degree to which a treatment plan is 'optimized' is in part determined by constraints placed on the planning algorithm." (*Id.*) "The user has direct control over two of these constraints: "aggressiveness" and "treatment time." (*Id.*)

C. Brief Description of Viggars

Viggars discloses the computer program "OSCAR," which "evaluates dose-volume histograms in a consistent way for use in 3-dimensional treatment planning." (Ex. 1015, Viggars at 419.) "Based on a dose prescription specified by a radiation oncologist, the technique provides a quantitative and easily understood visual analysis of a proposed dose distribution." (*Id.*)

Viggars explains that "Dose volume histograms (DVH) are a convenient way of summarizing the information in a 3-dimensional dose distribution." (*Id.* at 419.)

Viggars teaches that "[t]o realize the maximum benefit from the use of DVH's a technique is needed for comparing and evaluating them objectively and consistently" and that "[s]uch a technique would also enable them to be used in defining and ensuring adherence to a treatment protocol." (*Id.*) To achieve this benefit, Viggars "describe[s] 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." (*Id.* at 420.) "The technique provides visual and quantitative tools for the consistent evaluation and comparison of alternative treatment plans," including "objective score functions which quantify the deviation of the dose distribution from the dose prescription," 2-D "images of regret," and "histograms of regret, in either cumulative or differential form, which provide a striking and easily assimilated visual comparison of CDVH or DDVH with dose prescription." (*Id.*)

Viggars explains that "[t]he quality of a proposed plan may therefore be judged by how far its CDVH departs from the ideal histograms, and a dose prescription can be defined by specifying the maximum acceptable deviations from the ideal shape." (*Id.*) Viggars refers to such deviations as "regret." (*Id.*) The dose prescription of Viggars provides both overdose and underdose limits for the target as well as dose-volume criteria in the form of "maximum partial target volume" or "minimal partial target volumes" and dose-volume limits for the non-target tissue

and organs-at-risk. (*Id.* at 420-421.) "To provide a quantitative measure of how well a proposed treatment plan conforms to the dose prescription," Viggars defines "a set of score functions which compare the actual deviations of a plan from the ideal CDVH with the maximum deviations allowed by the dose prescription." (*Id.* at 422.) Viggars provides a specific score function, where the value indicates the quality of the dose distribution: "10 for an ideal distribution, zero at the limit of acceptability, and negative when the dose-volume limit is violated." (*Id.* at 423.)

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.)

Comparisons of the color-coded deviations between the DDVHs and CDVHs of a treatment plan and the ideal dose prescription for the target and an organ-at-risk

are depicted by Viggars' OSCAR program, as exemplified in Figure 3:

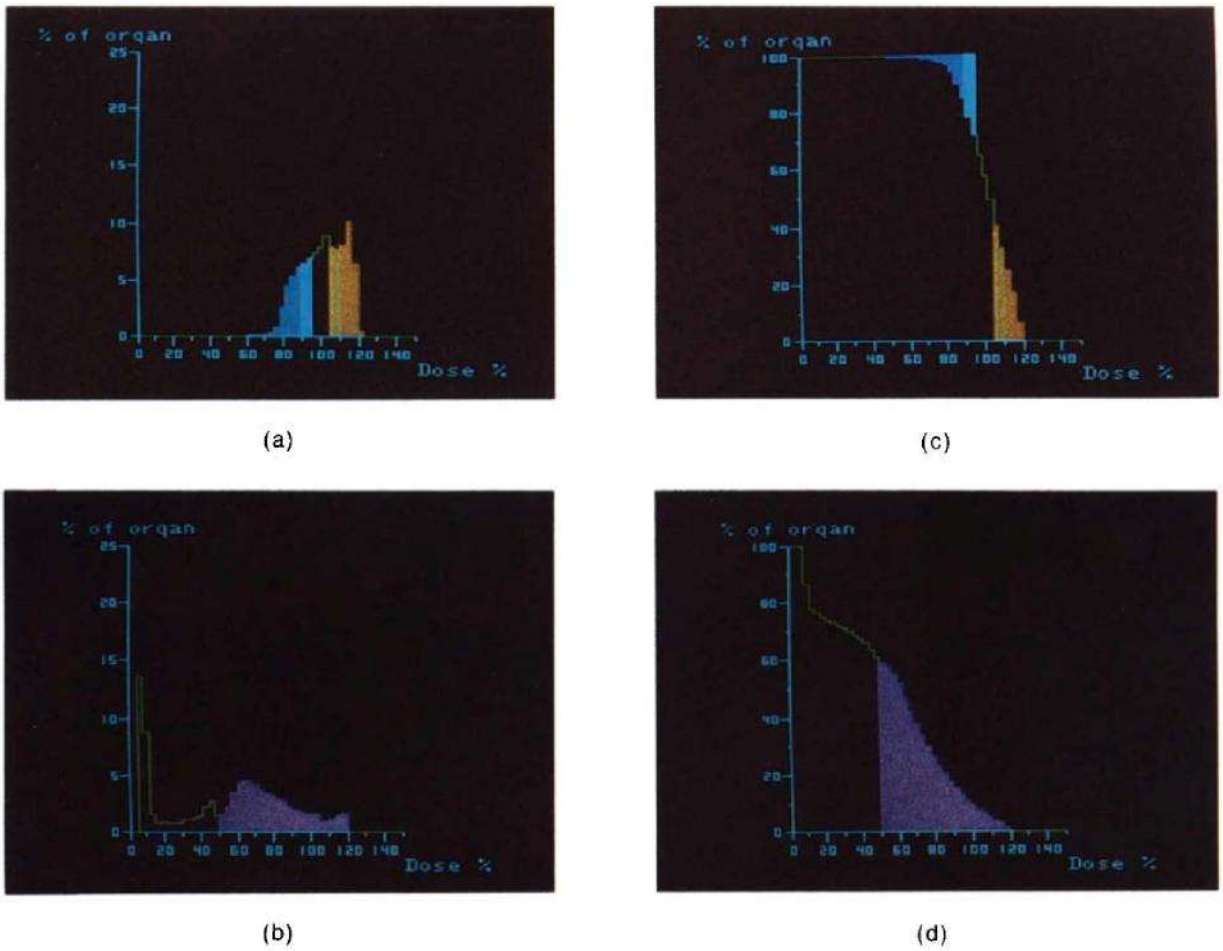


Fig. 3. Histograms of regret for an arbitrary dose distribution. DDVH for (a) the target and (b) a specific organ; and CDVH for (c) the target and (d) the same specific organ.

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

D. Motivation to Combine and Reasonable Expectation of Success

A POSA would have been motivated to use the OSCAR program of Viggars to evaluate the clinical acceptability of the "optimized" treatment plans calculated by Carol-1995's Peacock program to ensure that the plans comply with the radiation oncologist's dose prescription requirements. (Ex. 1002 ¶78.) Viggars expressly provides this motivation: "The power of the method is derived from the OSCAR

prescription which allows the clinician to express the needs of his or her patient in a simple quantitative way taking into account clinical experience." (Ex. 1015, Viggars at 426.)

A POSA would have further found the objective scoring and visual displays of Viggars' OSCAR program to be a desirable and facile way of evaluating the clinical acceptability of plans generated by the Peacock system of Carol-1995. As Viggars explains, the data supplied by the OSCAR program can be "used to decide, in an objective and systematic way, whether a particular [treatment] plan is acceptable." (Ex. 1015, Viggars at 425; Ex. 1002 ¶79.)

The benefits of Viggars quantitative plan scoring was, in fact, already recognized in the art as having "addressed the problem of basing a decision on the degree of acceptability of a treatment plan in terms of simple parameters." (Ex. 1008, Webb-1993(Book) at 20.) The art goes on to explain the benefits of the simple scoring parameters of Viggars to provide confidence in the acceptability of a clinically relevant treatment plan:

> The clinician is asked to provide a prescription, a series of targets and organs at risk together with the fractional volumes which may or may not be raised to certain tolerances. Provided the treatment planner derives a scheme with positive score function, the plan can be considered acceptable and in principle need not be shown to the clinician—the prescription having been met.

(*Id.* at 21.)

The prior art also recognized that in addition to "generating numerical scores, OSCAR combines the advantages of viewing 2D isodose distributions with the advantages of the dose-volume histogram." (*Id.*) Accordingly, a POSA would have recognized the benefits and advantages provided by the OSCAR program in evaluating treatment plans and would have had ample motivation to use OSCAR to assess and evaluate the computer-generated "optimal" treatment plans generated by by Carol-1995's Peacock system. (Ex. 1002 ¶81.)

A POSA would have expected success in combining the use of Viggars' OSCAR program with Carol-1995's Peacock planning optimization algorithm because the combination simply uses the established functions of each disclosed system. (Ex. 1002 ¶82.) That is, an "optimized" treatment plan could be generated as expressly taught by Carol-1995 using the Peacock system and this "optimized" plan would be used as input for evaluation by the OSCAR program of Viggars. (*Id.*) A POSA would have known how to conform the relevant files used by the Peacock planning system for input into the OSCAR program in a routine matter. (*Id.*)

Additionally, Viggars expressly teaches that the OSCAR program "has been developed on a commercial treatment planning system and has been fully integrated with the conventional software so that it can be ***used easily*** on a routine basis." (Ex. 1015, Viggars at 420 (emphasis added).) A POSA likewise would have been able to

integrate the OSCAR program of Viggars with the Peacock treatment planning system with a reasonable expectation of success. (Ex. 1002 ¶83.)

E. Claim 43

Claim 43 is an open "comprising" claim that is obvious over the combination of Carol-1995 and Viggars. Each element of the claimed method is disclosed, suggested, and/or otherwise obvious to a POSA in accordance the disclosures of the Peacock Plan of Carol-1995 and the OSCAR program of Viggars. (Ex. 1002 ¶84.)

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

To the extent the preamble is limiting, it is disclosed by Carol-1995. (Ex. 1002 ¶85.) Carol-1995 teaches a method for "conformal therapy—delivering a high dose of radiation in a spatial distribution conforming to the shape of the target volume while concomitantly decreasing the volume of the surrounding normal tissue receiving that same dose." (Ex. 1006, Carol-1995 at 56.) Carol-1995 discloses that with the Peacock three-Dimensional Conformal System "[t]he parameters driving beam modulation and field shaping are generated by a three-dimensional planning computer using a simulated annealing algorithm guided by cost functions which quantify prescribed treatment constraints." (*Id.*) As described in Carol-1995, the Peacock system "plans and implements" these "conformal treatment plans"

generated by a simulated annealing algorithm." (*Id.*)

2. "distinguishing each of the at least one tumor target volume and each of the at least one structure volume by target or structure type;"

This element is disclosed by both Carol-1995 and Viggars. (Ex. 1002 ¶86.) Carol-1995 discloses delivering "the prescribed dose to the ***identified*** target volume" while "keep[ing] the dose to avoidance volumes (volumes which should receive no radiation) and sensitive volumes (volumes which have a dose limit which is less than the dose to the target volume) below user-defined limits." (Ex. 1006, Carol at 57 (emphasis added).) Similarly, Carol uses a cost function that is "the sum of weighted costs for each structure and target," which necessarily requires performance of this step of claim 43. (*Id*.) Viggars teaches a dose prescription, as shown in Table 1, which distinguishes the target, sensitive organs, and non-target tissue. (Ex. 1015, Viggars at 421.) Accordingly, this step is also performed by Viggars.

Furthermore, a POSA would have found this element obvious because designating target and structure volumes by type is a fundamental step in the simulated annealing optimization techniques known in the prior art. (Ex. 1002 ¶87; *see, e.g.*, Ex. 1017, U.S. 5,596,619 (Fig. 10, Step 801).)

3. "determining desired partial volume data for each of the at least one target volume and structure volume associated with a desired dose prescription;"

Viggars teaches using "a dose prescription" that "can also be used as part of

the definition of a treatment protocol." (Ex. 1015, Viggars at 420.) Partial volume data, as defined by the '096 patent, "generally describes what percent of the volume of a tumor or structure can receive how much dose." (Ex. 1001 at 6:67-7:1.) Viggars discloses a dose prescription that uses "maximum partial target volume" and dose-volume limits for organs. (*Id.*) The dose prescription in Table 1 of Viggars are "expressed as a percentage of" target or structure volume. (Ex. 1015, Viggars at 421.) Thus, the dose prescription expressly disclosed and taught by Viggars satisfies this limitation. (Ex. 1002 ¶88.)

4. "entering the desired partial volume data into a computer;"

As discussed for the previous element, Viggars teaches using "a dose prescription" that is a form of partial volume data and "can also be used as part of the definition of a treatment protocol." (Ex. 1015, Viggars at 420.) It would have been inherent and obvious to one of ordinary skill in the art that the partial volume data in Viggars' dose prescription would have to be entered into the computer running the OSCAR program since the program relies on the entered dose prescription to perform the functions of quantitatively scoring a treatment plan and generating images and histograms of regret. (Ex. 1002 ¶9.) Accordingly, this limitation is obvious over Viggars.

5. "providing a user with a range of values to indicate the importance of objects to be irradiated;"

This limitation is obvious in view of the disclosures of Carol-1995 and the

knowledge of a POSA. (Ex. 1002 ¶90.) Carol-1995 "defines cost as the sum of weighted costs for each structure and target." (Ex. 1006, Carol-1995 at 57.) "The ***relative values*** of 'WeightI' (target weight) and 'WeightJ' (structure weights) emphasize or deemphasize the contribution of each target and structure to the total cost." (*Id*. at 58.) Further, "[t]he degree to which a treatment plan is 'optimized' is in part determined by constraints placed on the planning algorithm" and "***[t]he user has direct control*** over two of these constraints: 'aggressiveness' and 'treatment time.'" (*Id*. (emphasis added.)) For example, "'[a]ggressiveness' influences the ***relative importance*** of delivering the prescribed dose to the complete target versus sparing avoidance and sensitive structures (***relative values*** of 'WeightI' and 'WeightJ')." (*Id*. (emphasis added).) Thus, Carol-1995 teaches that in Peacock the user has "direct control" over the "aggressiveness" of an optimized plan based on the "relative values" of the importance factors "'Weight I' (target weight) and 'WeightJ' (structure weights)." (Ex. 1002 ¶91.)

Although Carol-1995 does not describe precisely how the user is provided with "direct control" over the "aggressiveness" based on the relative values of WeightI and WeightJ, it does generically disclose a "user interface" for "user interaction with the system" and to "input and process data." (Ex. 1006, Carol-1995 at 60; Ex. 1002 ¶91.) Since a POSA would have recognized (1) that control over "aggressiveness" is based on a relative values of WeightI/WeightJ and (2) that a user

interface is provided to "input" data, it would have been obvious to a POSA to provide the user with a range of "aggressiveness" values to select from. (Ex. 1002 ¶91.) Providing the user "direct control" over "aggressiveness" in this manner would have been obvious to a POSA in view of Carol-1995's teachings and satisfies this claim limitation. (Ex. 1002 ¶91.)

For example, a POSA would readily understand that the range of "aggressiveness" values would control "the relative importance of delivering the prescribed dose to the complete target versus sparing avoidance and sensitive structures," as expressly taught by Carol-1995. (Ex. 1002 ¶92.) In this regard, a POSA would understand that increasing WeightI relative to WeightJ would favor the target over sensitive structures and vice versa. (Ex. 1002 ¶92.) A POSA would therefore have found it obvious that a range of relative values for WeightI and WeightJ could be provided to the user to indicate the importance of objects to be irradiated. (Ex. 1002 ¶92.)

6. "providing the user with a range of conformality control factors; and"

Carol-1995 teaches that "[t]reatment time . . . is directly proportional to the number of arcs used in the treatment (in turn related to ***the number of table angles and the thickness of the treatment slice***) and ***roughly proportional to the degree of conformation*** which will result from implementing the plan." (Ex. 1006, Carol-1995 at 58 (emphasis added).) Accordingly, the number of table angles and the thickness

of the treatment slice are a range of conformality control factors taught by Carol-1995, and therefore satisfy this claim limitation. (Ex. 1002 ¶93.)

Carol-1995 further teaches plan optimization "with a single table angle employing a 1-cm-thick slice" and "a five-table angle radiosurgical treatment . . . using 5-cm-thick slices." (Ex. 1006, Carol-1995 at 60.) As such, a POSA would have recognized from Carol-1995 that the number of table angles and the thickness of the slice would be under the direct control of the user when identifying the constraints to be used during optimization. (Ex. 1002 ¶94; Ex. 1023, Carol-1994 at 108 ("constraints are placed on the system . . . the number of table angles and the thickness of the treatment beam").) A POSA therefore would have found it obvious to provide the user with a range of treatment angles (e.g., 1 to 5) and slice thicknesses (e.g., 1 cm to 5 cm) in the user interface to facilitate and simplify the user's entry of constraints when using the Peacock system, which also satisfies this claim element. (Ex. 1002 ¶94.)

7. "using the computer to computationally calculate an optimized radiation beam arrangement."

Carol-1995 states that "Peacock uses a so-called fast simulated annealing process to determine a set of beam weights" and is a "very computer-intensive process." (Ex. 1006, Carol-1995 at 57, 58.) Accordingly, Carol-1995's use of a computer to determine an optimized treatment plan using simulated annealing satisfies the claimed function and corresponding structure of "the computer to

computationally calculate an optimized radiation beam arrangement," as well as the term's ordinary meaning. (Ex. 1002 ¶95.)

F. Claim 44: "The method of claim 43 further comprising the step of applying the optimized radiation beam arrangement to the patient with a conformal radiation therapy apparatus."

Carol-1995 discloses the obvious goal of using a clinically acceptable optimized treatment plan for patient treatment. (Ex. 1002 ¶96; *see, e.g.*, Ex. 1017 U.S. 5,596,619 (Fig. 10, Step 808).) "The Peacock three-Dimensional Conformal System plans and implements . . . conformal treatment plans." (Ex. 1006, Carol-1995 at 56.) "Patient treatments with Peacock began in March 1994," and "eight patients had been treated as of September 1994." (*Id*. at 61.) Thus, Carol-1995 discloses this limitation.

G. Claim 46: "The method of claim 44 wherein the optimized radiation beam arrangement is calculated using different cost function parameters depending on the target or structure type."

This limitation is taught by Carol-1995. (Ex. 1002 ¶97.) Carol-1995 explains that Peacock "defines cost as the sum of weighted costs for each structure and target." (Ex. 1006, Carol-1995 at 57.) "For targets, cost is the mean-squared difference between realized dose and prescribed dose. For structures, cost is the mean-squared difference between realized dose and zero dose." (*Id.*) The cost function parameters in Peacock are different between targets and structures because the cost to the target is evaluated based on the minimum dose parameter, whereas

structures are not. (Ex. 1002 ¶97.) Additionally, Carol teaches that within the cost function "[t]he relative values of 'WeightI' (target weight) and 'WeightJ' (structure weights) emphasize or deemphasize the contribution of each target and structure to the total cost." (*Id*. at 58.) The "WeightI" and "WeightJ" are different cost function parameters depending on the target or structure type used to calculate the optimized beam arrangement. Accordingly, Carol-1995 teaches this limitation. (Ex. 1002 ¶97.)

XII. GROUND 2: CLAIMS 43, 44, AND 46 ARE OBVIOUS OVER CURRAN-5 IN VIEW OF CAROL-2

A. Prior Art and Date Qualification

Each limitation of claims 43, 44, and 46 is disclosed or suggested by the combination of Curran, *Chapter 5 – Conformal Radiation Therapy Using a Multileaf Intensity Modulating Collimator*, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 75-90 (Ex. 1007) **("Curran-5")** and Carol, *Chapter 2 - IMRT: Where we are today*, The Theory & Practice of Intensity Modulated Radiation Therapy (1997) 17-36 (Ex. 1020) ("**Carol-2**").

Both Curran and Carol-2 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 Curran-5 and Carol-2 "is available now." (Ex. 1004, Butler Decl. Ex. A at 008.) 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 Curran-5 and Carol-2 was also publicly available for purchase as of at least April 12, 1997. (Ex. 1004, Butler Decl. Ex. A at 019.) Moreover, the book bears a copyright date of 1997 (Ex. 1020 at 3.) 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 19, 1998 date-stamped copy of the book. (Ex. 1003 (Hall-Ellis Decl.) ¶64.)

Neither Curran-5 nor Carol-2 was before the Examiner during prosecution.

B. Brief Description of Curran-5

Curran-5 discloses the use of the "MIMic" multileaf collimator with the PEACOCK System and using plans calculated by the PEACOCK Plan treatment planning program. (*See* Ex. 1007, Curran-5 at 75-77.) Curran-5 explains that "PEACOCK Plan provides tools for assisting the user in defining the anatomy of interest for inverse treatment planning, entering the prescription needed to define the treatment goals, and analyzing the resultant dose distribution to determine how closely the planning system and MIMiC treatment will be in in meeting the prescription goals." (Ex. 1007 at 80.) "The system also integrates the use of

simulated annealing optimization and a cost function for determining the optimal plan." (*Id.* at 80-81.) "The PEACOCK Plan system divides the treatment planning process into a number of distinct steps, each with their own set of tools and displays" including "defining the anatomy, entering the prescription, [and] calculation of the optimal plan." (*Id.* at 81.)

C. Brief Description of Carol-2

Carol-2 describes various aspects of the clinical implementation of IMRT treatment plans, as well as specific details regarding the "PEACOCK intensity modulated radiation therapy (IMRT) system." (*See* Ex. 1020, Carol-2 at 17.) 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 the 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 resolve; a higher cost is produced when the resulting dose distribution strays from the desired dose distribution.

(Ex. 1020, Carol-2 at 20.)

Carol-2 states that the "PEACOCK Plan uses an interface which involves assigning graded weights and priorities to the structures and targets in order to achieve desired results." (Ex. 1020, Carol-2 at 21.) "By adjusting the relative importance of the target and the surrounding structures in the planning process, the

planning system would generate plans which would vary greatly in the degree to which sensitive structures are spared and high dose lines conform to the 3D target contour." (*Id.*) Carol-2 discloses that the user "performs target and structure segmentation with PEACOCK" and "***the prescription (partial volume data) is entered into the system***." (*Id.* at 22 (emphasis added).)

D. Motivation to Combine and Reasonable Expectation of Success

A POSA would have been motivated to combine the teachings of Curran-5 with Carol-2 because they both describe the same PEACOCK System and PEACOCK Plan radiotherapy treatment planning program. (Ex. 1002 ¶105.) Both references address using PEACOCK for the optimization a treatment plan for conformal radiotherapy. (*Id.*)

It would also have been obvious to a POSA that the disclosures from the same book, at the same time, describing features of the same system would be combined in order to obtain a more complete understanding of the PEACOCK System being described. (*Id.*) For instance, a POSA would have been motivated to combine the references in order to obtain a deeper understanding of the implementation details of the PEACOCK System in general and PEACOCK Plan treatment planning program according to the disclosures in Curran-5 and Carol-2. (*Id.*) For example, PEACOCK Plan allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (Ex. 1007,

Curran-5 at 85.) Carol-2 merely clarified the prescription is entered into the system as "partial volume data." (Ex. 1020, Carol-2 at 22.)

One of ordinary skill in the art would have understood that there was a reasonable expectation of success in combining the relevant PEACOCK System and PEACOCK Plan disclosures in Curran-5 and Carol-2 because they both describe the same system and computer program already being used within the field. (Ex. 1002 ¶107.)

E. Claim 43

Claim 43 is obvious over the combination of Curran-5 and Carol-2. (Ex. 1002 Curran-5 discloses, suggests, or renders obvious all elements of claim 43 with the exception of the "partial volume data" limitations, which are disclosed, suggested, and/or obvious based on the disclosures of Carol-2. (*Id.*)

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

To the extent the preamble is limiting, it is disclosed by Curran-5. (Ex. 1002 ¶109.) Curran-5 teaches that "Peacock Plan is a planning system" that "integrates the use of simulated annealing optimization and a cost function for determining the optimal plan." (Ex. 1007, Curran-5 at 80-81.) Curran-5 further explains that PEACOCK Plan "allow[s] the user to design the desired dose distribution, then

allow[s] the computer to do the trial and error calculations to find the optimal method for delivering the prescription." (*Id.* at 80.) PEACOCK Plan also allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (*Id*. at 85.) MIMiC, used "in conjunction with" PEACOCK Plan, can "deliver a highly conformal radiation treatment using a set of rotational beams and table positions." (*Id.* at 75.) Additionally, a POSA would have understood that the teachings of Curran-5 with respect to the PEACOCK Plan program were describing a system used to perform inverse treatment plan optimization, as PEACOCK was well known to a person of ordinary skill in the art. (Ex. 1002 ¶109.) Thus, Curran-5 teaches this limitation.

2. "distinguishing each of the at least one tumor target volume and each of the at least one structure volume by target or structure type;"

Curran-5 discloses that "[p]erhaps the most important phase of PEACOCK Plan is the anatomy phase, where the targets (areas of the patient where a target or prescription dose is defined) and sensitive structures (areas of the patient where a maximum or limit dose is defined) are created by the user." (Ex. 1007, Curran-5 at 83.) "Information on these regions is used by the calculation routines to determine the optimal plan." (*Id.*) "Once all sensitive structures and targets have been defined by the planner, and the entire image set viewed, the anatomy can be approved, allowing the user to move on to the prescription phase." (*Id*. at 84.) Thus, Curran

discloses this limitation. (Ex. 1002 ¶110.)

3. "determining desired partial volume data for each of the at least one target volume and structure volume associated with a desired dose prescription;"

Curran-5 discloses that "PEACOCK Plan provides tools for assisting the user in . . . entering the prescription needed to define the treatment goals." (Ex. 1007, Curran-5 at 80.) PEACOCK Plan allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (*Id*.) Carol-2 teaches that in PEACOCK Plan "the prescription (***partial volume data***) is entered into the system." (Ex. 1020, Carol-2 at 22.) In order for the partial volume data prescription to be *entered* into the system, it necessarily requires (or is at least obvious to a POSA) that the step of *determining* the partial volume data for the dose prescription had already been performed. (Ex. 1002 ¶111.) Thus, the combination of Curran-5 and Carol-2 teaches this limitation. (*Id.*)

4. "entering the desired partial volume data into a computer;"

Curran-5 discloses that "PEACOCK Plan provides tools for assisting the user in . . . entering the prescription needed to define the treatment goals." (Ex. 1007, Curran-5 at 80.) PEACOCK Plan allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (*Id*.) Carol-2 teaches that in PEACOCK Plan "the prescription (***partial volume data***) is entered into the system. (Ex. 1020, Curran-2 at 22.) Curran-5 further provides an

image showing the user interface used to enter the partial volume data prescription into a computer:

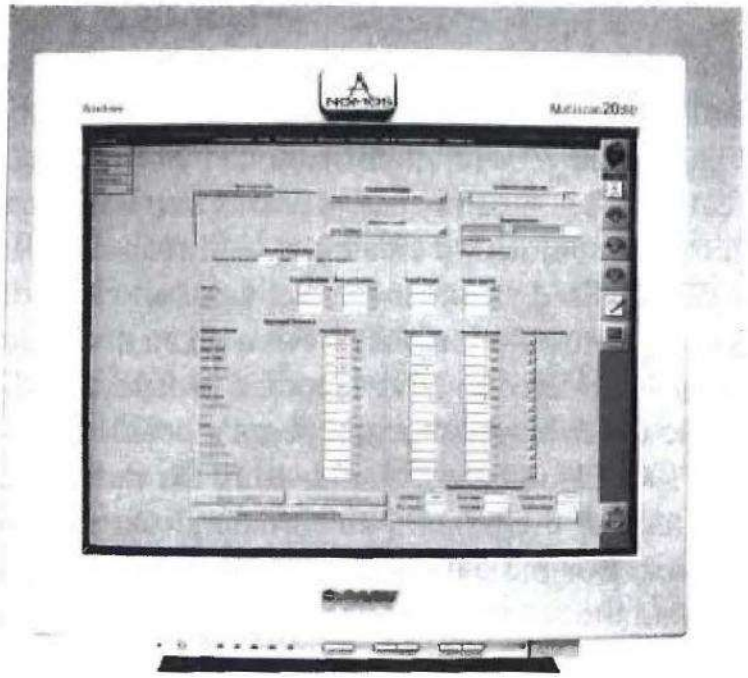


Figure 10. Prescription definition.

(Ex. 1007, Curran-5 at 85.)

Thus, the combination of Curran-5 and Carol-2 teaches this limitation. (Ex. 1002 ¶¶112-113.)

5. "providing a user with a range of values to indicate the importance of objects to be irradiated;"

Curran-5 discloses that "the user will see default values for all appropriate fields on the prescription form," including the weights on PEACOCK's planning parameters section. (Ex. 1007, Curran-5 at 84.) Curran further explains that "[t]he weights determine the relative importance of the various defined areas during the optimization" and "[a] target or structure with a high weight will have its goals met

more closely than one with a lower value." (*Id*. at 85.) Curran-5 states that "[t]ypical weights are from 0.0 (don't include in optimization) to 2.0 (very important)." (*Id*.) Thus, Curran-5 provides a range of values for a user to indicate the importance of objects to be irradiated in PEACOCK Plan. (Ex. 1002 ¶114.) Accordingly, Curran-5 teaches this limitation.

6. "providing the user with a range of conformality control factors; and" (43[e])

Curran-5 teaches "treatment complexity" factors and an "aggressiveness slider" that satisfies this claim limitation. (Ex. 1002 ¶114.) For example, Curran-5 discloses that "[t]reatment complexity allows the user to select the thickness of the MIMiC slices used for delivery, as well as the number of table angles that will be considered during the calculation and optimization." (Ex. 1007 at 84.) Curran-5 also discloses that "[t]he aggressiveness slider allows multiple sets of defaults to be entered for a given structure set, according to the aim of the treatment (***highly conformal***, efficient delivery, etc.)." (*Id*. at 84-85 (emphasis added).) A POSA would have recognized that the thickness of the slices, number of table angles, and the aggressiveness slider would each affect the conformity of the optimized treatment plan, and therefore provide the user with a range of conformity control factors. (Ex. 1002 ¶114.)

7. "using the computer to computationally calculate an optimized radiation beam arrangement."

Curran-5 teaches using PEACOCK Plan running on a computer "to find the optimal method for delivering the prescription." (Ex. 1007, Curran at 80.) Curran-5 discloses that PEACOCK uses "simulated annealing optimization and a cost function for determining the optimal plan." (*Id.* at 80-81.) Accordingly, Curran-5's disclosure of the use of a computer that performed the claimed function with the corresponding simulated annealing algorithm of "the computer to computationally calculate an optimized radiation beam arrangement" satisfies this element under means-plus-function claiming. (Ex. 1002 ¶115.) The limitation would also be met under the limitation's plain meaning. (*Id.*)

F. Claim 44 "The method of claim 43 further comprising the step of applying the optimized radiation beam arrangement to the patient with a conformal radiation therapy apparatus."

Curran-5 discloses the PEACOCK System and equipment that can "deliver a highly conformal radiation treatment using a set of rotational beams and table positions." (Ex. 1007, Curran-5 at 75.) Further, Curran-5 discloses that:

> The PEACOCK System, including both MIMiC and PEACOCK Plan, ***has now been in use for more than two years at a number of sites***. These sites have performed extensive verification of the MIMiC delivery technique as well as the dosimetric accuracy of Peacock Plan. The results of this experience show the MIMiC to be a safe, reliable mechanism for conformal radiation therapy.

(*Id*. at 90 (emphasis added).) Thus, Curran-5 discloses this limitation. (Ex. 1002 ¶116.)

G. Claim 46: "The method of claim 43 wherein the optimized radiation beam arrangement is calculated using different cost function parameters depending on the target or structure type."

Curran-5 teaches that "the user will see default values for all appropriate fields on the prescription form," including the weights on PEACOCK's planning parameters section. (Ex. 1007, Curran-5 at 84.) Curran-5 further explains that "[t]he weights determine the relative importance of the various defined areas during the optimization" and "[a] target or structure with a high weight will have its goals met more closely than one with a lower value." (*Id*. at 85.) Accordingly, Curran-5 teaches this limitation by assigning different weights to determine the relative importance of the targets and structures. (Ex. 1002 ¶117.)

XIII. GROUND 3: CLAIMS 43, 44, AND 46 ARE OBVIOUS OVER CURRAN-5 IN VIEW OF CAROL-17

A. Prior Art and Date Qualification

Each limitation of claims 43, 44, and 46 is disclosed or suggested by the combination of Curran-5 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")**.

Carol-17 is prior art to the '096 patent for the same reasons that Curran-5 and Carol-2 as disclosed in Ground 3 above because Carol-17 is another chapter from

the same published book (The Theory & Practice of Intensity Modulated Radiation Therapy).

B. Brief Description of Carol-17

Carol-17 describes certain state of the art features of IMRT and identifies additional technological advancements within the field. (Ex. 1021, 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. (*Id.* 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.*)

C. Motivation to Combine and Reasonable Expectation of Success

A POSA would have been motivated to combine the teachings of Curran-5 with respect to the PEACOCK System with the teachings of Carol-17, such as those describing the CORVUS inverse planning system. (Ex. 1002 ¶121; Ex. 1021, Carol-17 at 247.) Curran-5 and Carol-17 are in the same field of intensity modulated radiotherapy treatment (IMRT), both describe inverse treatment planning programs (PEACOCK and CORVUS), and both are included within the same IMRT book. A POSA would have looked to the implementations of the two systems described in Curran-5 (PEACOCK) and Carol-17 (CORVUS) and motivated to incorporate any

of the improved or more beneficial features of CORVUS into the PEACOCK planning system. (Ex. 1002 ¶121.) A POSA would have reasonably expected to successfully combine the teachings of Curran-5 with Carol-17 because modifying the existing PEACOCK Plan to incorporate features taught by CORVUS would have been well within the capabilities of a POSA. (Ex. 1002 ¶121.)

For example, a POSA would have been motivated to utilize the advanced user interface and partial volume data prescription of CORVUS within the PEACOCK Plan system. (Ex. 1002 ¶122.) 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. (Ex. 1021, Carol-17 at 247.) Carol-17 further teaches that, over time, the "way of entering desired dose information" changed because "[c]linicians have begun to learn to 'think' in terms of partial volumes: 'What percent of the sensitive structure can I take to what dose before I begin to compromise its function?" (*Id.*) "It 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*.) 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.*) A person of ordinary skill in the art would have recognized these stated benefits of the CORVUS system and would have been

motivated to improve the PEACOCK system—to the extent it was not already within the system—by incorporating the prescription user interface for entering partial volume data of CORVUS. (Ex. 1002 ¶122.)

A POSA would have had a reasonable expectation of success in providing a prescription page in the PEACOCK Plan program taught by Curran-5 that includes partial volume data as taught by the CORVUS interface of Carol-17. (Ex. 1002 ¶123.) As Curran-5 discloses, PEACOCK Plan allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (Ex. 1007, Curran-5 at 85.) A POSA would have understood, from the teachings of Carol-2, that with PEACOCK Plan "the prescription (partial volume data) is entered into the system." (Ex. 1020, Carol-2 at 22.) Accordingly, a POSA would have understood that the PEACOCK Plan already incorporates a user interface for entering partial volume data of a prescription. (Ex. 1002 ¶123.)

Nevertheless, to the extent it would be required at all, a POSA would have found it routine to modify the PEACOCK Plan prescription user interface to allow for the entry of partial volume data as it would merely require the routine construction of data cells within the interface for each constraint of the partial volume data prescription. (Ex. 1002 ¶124.) Carol-17 teaches that in CORVUS, "[f]or each target, the user enters: goal, minimum dose, maximum dose and percent volume which is allowed to be underdosed" and "[f]or each structure, the user enters: desired

limit, minimum does, maximum dose and percent volume that can be greater than limit." (Ex. 1021, Carol-17 at 247.) A POSA would have found the construction of a user interface for entry of these parameters a straightforward task. (Ex. 1002 ¶124.)

One of ordinary skill in the art would have also been motivated to incorporate the partial volume prescription data of Carol-17 to enhance the utility of the visual displays of the PEACOCK System. (Ex. 1002 ¶125.) Curran-5 teaches that PEACOCK displays the results of the simulated annealing optimized plan by "show[ing] the user the cumulative dose volume histogram (CDVH) for the calculation." (Ex. 1007, Curran-5 at 88, Fig. 12.) A POSA would have found it advantageous for the clinician's evaluation of an optimized treatment plan to include "***a visual display of the prescribed dose limits on the CDVH***" based partial volume data. (Ex. 1002 ¶125; Ex. 1015, Viggars at 420 (emphasis added).) Such a graphical representation of partial volume data on a CDVH was recognized in the prior art as a simple and beneficial way to determine the clinical acceptability of a treatment plan:

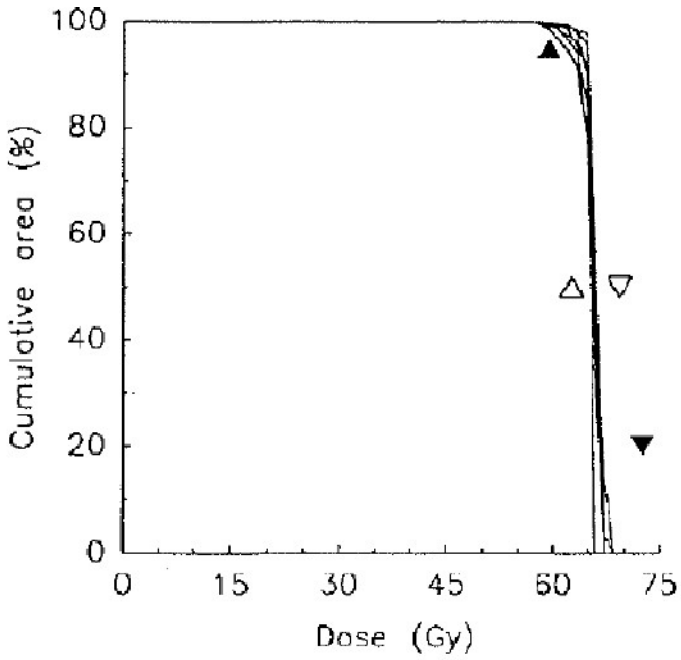
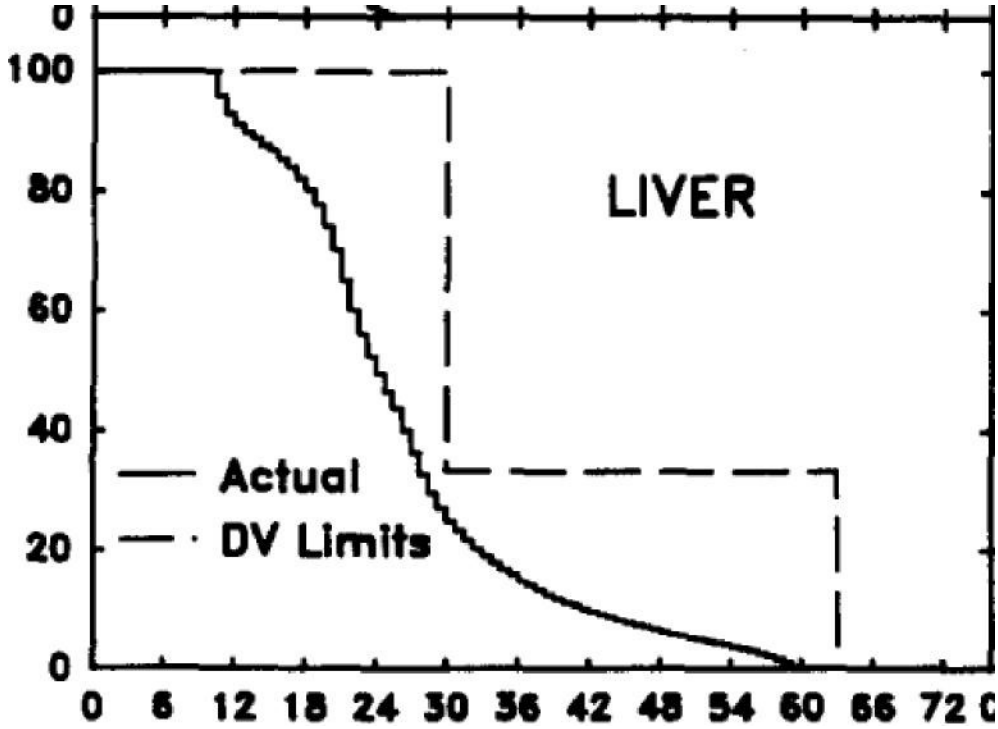


Figure 1.11. *Cumulative dose–area histogram for a mid-plane target region in seven patients with adenocarcinoma of the prostate. The inverted triangles represent tolerance points for target overdose and the upright triangles are tolerance points for target underdose. Open symbols are mild; closed symbols are severe tolerances. Note the histogram weaves between these constraints. This demonstrates a satisfactory treatment plan has been found (from Hahn et al (1990)) (reprinted with permission from Pergamon Press Ltd, Oxford, UK).*

(Ex. 1008, Webb-1993(Book) at 21 (emphasis added).)

Additionally, a POSA would further have recognized that the partial volume data constraints of CORVUS could also be used to construct a binned CDVH or CDVH curves that could be overlaid onto the CDVH curves for the treatment plans generated by PEACOCK to, again, help in the visual assessment of the acceptability of the "optimized" plan. (1002 ¶126.) The CDVH's of proposed treatment plans are commonly depicted in the same chart with the binned partial volume CDVH of a

dose prescription, such as for example, in the following where the solid line is the plan "optimized" CDVH and the dashed line is the histogram calculated from the dose-volume constraints:



(*See* Ex. 1031, Morrill-1991 at 1204 (Fig. 3); Ex. 1002 ¶126.)

Carol-17 teaches that the CORVUS "system creates CDVH curves for the targets and structures from" the entered partial volume data." (Ex. 1021, Carol-17 at 247.) A POSA would likewise have been motivated to allow enhanced evaluation of how well an "optimized" PEACOCK treatment plan corresponds with the partial volume data of the prescription by likewise overlay both CDVH curves (optimized and prescribed) in the same display. (Ex. 1002 ¶127.)

A POSA would have had a reasonable expectation of success in generating

the foregoing graphical displays including both CDVHs for an "optimized" PEACOCK Plan and the partial volume constraints or associated CDVHs of the CORVUS prescription. (Ex. 1002 ¶128.) The PEACOCK Plan included the capability of displaying the CDVHs for the "optimized" plan, and it would have been a trivial matter to include data points representing the prescribed partial volume constraints or CDVHs (binned or curves) within the display. (*Id.*)

D. Claim 43

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

For the same reasons as stated in Ground 2, to the extent this preamble is a claim limitation, is satisfied by Curran-5.

2. "distinguishing each of the at least one tumor target volume and each of the at least one structure volume by target or structure type;"

For the same reasons as stated in Ground 2, this limitation is satisfied by Curran-5.

3. "determining desired partial volume data for each of the at least one target volume and structure volume associated with a desired dose prescription;"

Curran-5 and Carol-17 inherently discloses and renders obvious this limitation. (Ex. 1002 ¶131.) Curran-5 discloses that "PEACOCK Plan provides tools for assisting the user in . . . entering the prescription needed to define the treatment

goals." (Ex. 1007, Curran-5 at 80.) PEACOCK Plan allows the user to enter "[t]he desired prescription doses for the targets (up to three) and limit doses to sensitive structures (up to 13)." (*Id*.) A POSA would have known that in the PEACOCK Plan "the prescription (***partial volume data***) is entered into the system," and therefore would have found it obvious from Curran-5's teachings that the prescription entered into PEACOCK includes partial volume data for the target and structures. (Ex. 1020, Carol-2 at 22; Ex. 1002 ¶131.)

Carol-17 discloses the CORVUS planning system, which "uses partial volume information for each structure out of which CDVH curves are generated and used as the goal by the optimizer." (Ex. 1021, Carol-17 at 247.) Carol-17 teaches that in CORVUS, "[f]or each target, the user enters: goal, minimum dose, maximum dose and percent volume which is allowed to be underdosed" and "[f]or each structure, the user enters: desired limit, minimum does, maximum dose and percent volume that can be greater than limit." (*Id.* at 247.)

Accordingly, Curran-5 and Carol-17 teach that the use of PEACOCK or CORVUS, respectively, includes the user entering prescribed partial volume data for the target and structures. (Ex. 1002 ¶133.) In order for the partial volume data prescription to be *entered* into the systems, it necessarily requires (or is at least obvious to a POSA) that the step of *determining* the partial volume data for the dose prescription had already been performed. (*Id*.) Thus, both Curran-5 and Carol-17

teach this limitation. (*Id.*)

4. "entering the desired partial volume data into a computer;" As set forth with respect to the previous claim element, Curran-5 and Carol-

As set forth with respect to the previous claim element, Curran 5 and Carol-17 teach that the use of PEACOCK or CORVUS, respectively, includes the user entering prescribed partial volume data into the user interface of a computer. (Ex. 1002 ¶134.) Accordingly, both Curran-5 and Carol-17 teach this limitation. (*Id.*)

5. "providing a user with a range of values to indicate the importance of objects to be irradiated;" (43[d])

For the same reasons as stated in Ground 2, this limitation is satisfied by Curran-5.

6. "providing the user with a range of conformality control factors; and" (43[e])

For the same reasons as stated in Ground 2, this limitation is satisfied by Curran-5.

7. "using the computer to computationally calculate an optimized radiation beam arrangement." (43[f])

For the same reasons as stated in Ground 2, this limitation is satisfied by Curran-5.

E. Claim 44: "The method of claim 43 further comprising the step of applying the optimized radiation beam arrangement to the patient with a conformal radiation therapy apparatus."

Curran-5 discloses the PEACOCK System and equipment that can "deliver a

highly conformal radiation treatment using a set of rotational beams and table positions." (Ex. 1007, Curran-5 at 75.) Further, Curran discloses that:

> The PEACOCK System, including both MIMiC and PEACOCK Plan, ***has now been in use for more than two years at a number of sites***. These sites have performed extensive verification of the MIMiC delivery technique as well as the dosimetric accuracy of Peacock Plan. The results of this experience show the MIMiC to be a safe, reliable mechanism for conformal radiation therapy.

(*Id*. at 90 (emphasis added).) Thus, Curran-5 discloses this limitation. (Ex. 1002 ¶138.)

The use of the CORVUS interface for entering the partial volume data and using that partial volume data to facilitate and improve the visual assessment of CDVHs associated with an "optimal" treatment plan generated by PEACOCK under the combination of this obviousness ground would not alter the disclosed and otherwise obvious use of optimized PEACOCK Plans for patient treatment. (Ex. 1002 ¶139.) First, a POSA would have known that PEACOCK Plan already used partial volume data as part of its prescription. (*Id.*) Second, the proposed combination would actually bolster the ability to confirm the clinical acceptability of PEACOCK Plans by displaying the optimized CDVHs against the dose prescription partial volume criteria in a single display. (*Id.*)

F. Claim 46: "The method of claim 43 wherein the optimized radiation beam arrangement is calculated using different cost function parameters depending on the target or structure type."

Curran-5 discloses that "the user will see default values for all appropriate fields on the prescription form," including the weights on PEACOCK's planning parameters section. (Ex. 1007, Curran-5 at 84.) Curran further explains that "[t]he weights determine the relative importance of the various defined areas during the optimization" and "[a] target or structure with a high weight will have its goals met more closely than one with a lower value." (*Id*. at 85.) Curran-5 further explains that "[t]ypical weights are from 0.0 (don't include in optimization) to 2.0 (very important)." (*Id*.) Accordingly, Curran-5 teaches this limitation by assigning different weights to determine the relative importance of the targets and structures. (Ex. 1002 ¶140.)

XIV. CONCLUSION

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

Dated: May 28, 2020

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. §42.24(d), the undersigned certifies that the foregoing Petition for *Inter Partes* Review of U.S. Patent No. 6,393,096 contains, as measured by the word-processing system used to prepare this paper, 11,287 words. This word count does not include the items excluded by 37 C.F.R. §42.24 as not counting towards the word limit.

Dated: May 28, 2020

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CERTIFICATE OF SERVICE

The undersigned certifies pursuant to 37 C.F.R. §42.6(e) and §42.105 that on May 28, 2020, a true and correct copy of the foregoing **PETITION FOR INTER PARTES REVIEW**, including all supporting **EXHIBITS**, and Petitioner's **POWER OF ATTORNEY** are being served on the Patent Owner and counsel of record for the Patent Owner, via electronic mail and via Federal Express Overnight at the correspondence address of record as listed on PAIR:

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