PHYSICS AND CLINICAL APPLICATION OF IMRT / IGRT , RADIOSURGEY AND SBRT

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- Intensity Modulated Radiation therapy (IMRT)
- Image Guided Radiotherapy (IGRT)
- Stereotactic Radio Surgery (SRS)
- Stereotactic Body Radiosurgery (SBRT)



What is IMRT ?

- Intensity-modulated radiation therapy (IMRT) is an advanced form of <u>three-dimensional conformal radiotherapy</u> (3DCRT)
- The purpose of IMRT is to shape isodose lines by varying beam intensity in order to conform to clinical requirement



IMRT Advantages

- Conformality
 - Concave shaped dose distribution
- OAR sparing with sharp dose fall-off
- Dose escalation
- Lower rate of complication
 - Reduced cost of patient care
- SIB

The Magic Bullet "Conformality"



IMRT Methods

· 76~	Intensity modulation method
Segmental MLC (step and shoot)	During Beam On , MLC, Table & Collimator stationary. Each gantry angle multiple segments
Dynamic MLC (sliding window)	MLC move while beam on.
Intensity-modulated arc therapy (IMAT or VMAT or Rapid ARC)	MLC move while the gantry is rotating.
Serial tomotherapy	Gantry rotates around the patient with the couch fixed. Binary leaves modulate a fan beam. Upon completion of each rotation, the couch is moved in a step-wise fashion
Helical tomotherapy	Gantry and couch move synchronously. Binary leaves modulate a fan beam

REQUIREMENTS FOR IMRT

- Medical Linear Accelerator
- MLC
- Necessary software
- QA equipments



Terminology

• DMLC

 IMRT delivery mode in which leaves continuously move and shape the beam intensity while the radiation is turned on.

• SMLC

 IMRT delivery mode in which leaves only move when the radiation beam is turned off and remain in pre-defined position while the required radiation doses are being delivered.

• Segment (control point)

- Shaped aperture formed by MLCs with uniform beam intensity;



Score

 Numeric value of the objective function that represents a figure of merit indicating the quality of a treatment plan.

• Forward planning

 Trial and error method where the treatment fields or beam weights are modified iteratively to achieve acceptable clinical solution.

Inverse planning

 Optimization process that translates mathematical formalism of clinical requirements into deliverable intensity patterns.

Class solution

 Use of clinical experience based on solving similar cases with the same treatment technique or the same approach.

Iterations:

executing the same set of instructions a given number of times or until a specified result is obtained

Process of IMRT

6 steps

- Immobilization
- Simulation
- Target delineation
- Treatment planning and optimization
- Quality assurance
- Treatment delivery

Physics Components of IMRT

ASTRO recommendations for Patient selection

- Situations requiring IMRT
 - Irregular target
 - Close proximity to critical structure
 - IMRT only option to cover volume with narrow margin to protect adjacent structures
 - Nearby previously irradiated area
 - Conformal dose distribution required for concave treatment target



Immobilization accessories

- Air equivalent (low density)
- Neck rest and base plate



Delineation of target

- Use of clinical information and multiple imaging modalities
- GTV, CTV and PTV



Delineation of OARs

- OARs : parallel and series
- Parallel: parotids, ears, TMJs, duodenum, liver, GI
- Series: spinal cod, brainstem, optic chiasm, nerves, lens, brain, eyes, mandible, temporal lobes
- For serial organs, Planning organ at risk volume(PRV) should be delineated

Planning risk volumes (PRV)

- PRV
- spinal cord/brain stem
- Uninvolved parotid glands



Remaining volume at risk

- Structures not included in CTV or OARs should be delineated as remaining volume at risk (RVR)
- Dose constraints to RVR avoids unsuspected high dose regions
- Is useful to estimate the late effects of irradiation specially carcinogenesis



Buildup region

- Important when target regions (PTV) extend into the buildup region.
- Calculated doses are often inaccurate and lower than delivered doses.



Buildup region

Likely to cause hot spots in the target and elsewhere as a result of inverse planning engine fighting with the buildup effect – may cause excessive skin reactions and compromise the plan quality.



Treatment planning & optimization



Planning

Forward Planning

from field definition to dose distribution



Dose calculation

Dose distribution

Dose delivery with uniform radiation intensity Inverse Planning from dose distribution to field definition

> Dose delivery with non-uniform radiation intensity

Leaf sequence generation

Optimization

T/t goals (Objective Function)

Beam selection

- Basic principles
 - Choosing the shortest pathway to irradiate the tumour
 - Avoiding direct irradiation to the critical structures
 - Keeping a large beam separation as possible
 - Two parallel opposed beams not used they provide less beam variables for optimization



Beam Placement

• Depends on target shape and location



Beam Angle Optimization

 Optimum beam angles can be derived by using beam angle optimization available with TPS

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Planning Objectives (Constraints)

Ideal objectives

- PTV
 - Lower objective:
 - 100% volume = 100% prescription dose
- Upper objective:
 - None of PTV volume receive more than 100% dose
- OAR
- None of the OAR volume receive any dose
- Non realistic:
 - Never practically achievable



Planning Objectives (Constraints)

Realistic objectives

- PTV
- Lower objective
 - 100% volume = 95% prescription dose
- Upper objective
 - None of PTV volume receive more then 108% of prescription dose
- OAR (serial organs)
- None of the OAR volume receive more then tolerance dose



Optimization

Definition:

Systematic computerized process to generate a large number of plans rapidly and to evaluate and rank them according to some specified criteria

Optimization

Optimization Criteria (Objective Functions & Constraints) Optimization Process (Algorithms)

Dose calculation algorithms

Correction Based algorithms

Pencil beam algorithm



- Convolution superposition
- Monte Carlo



Pencil beam algorithm

- Correction based model depend on empirically measured data for a limited number of situations.
- Correct the dose distribution for the presence of the beam modifiers, contour corrections, tissue heterogeneities, scatter and other issues encountered in treatment planning of real patients.

Bourland, Chaney and Ostapiak

The dose at a point resulting from each individual beamlet is calculated using the product of

- constants
- MUs delivered
- Inverse square law
- Tissue-Maximum Ratio (TMR)
- Output factor
- Transmission factor
- Off-axis ratio
- Total dose at a point is summation of doses contributed by individual pencil beams
- This kind of simplicity offer significant speed advantages for use in the optimization code

 But, have limited accuracy particularly for 3D heterogeneity correction in lung and tissue interfaces especially when electronic equilibrium is not fully

established.





Central axis 4 MV X-ray depth-dose curves computed for a variety of field sizes in a water phantom with a lung-equivalent slab (0.3 g/cm3)

Model based algorithms

- Compute dose distribution with a physical model which **simulates** the actual radiation transport.
- Simulation of transport of Primary photon, scattered photons and electrons separately.

- Convolution-Superimposition
- Monte-Carlo

Convolution superposition algorithms

- Based on the kernel-based models, which directly measure or compute the dose in a phantom or patient.
- Primary photon transport simulation as well as Kernel computation can be done using Monte Carlo code(EGS4)
- Takes into account beam energy, geometry, beam modifiers, patient contour, and electron density distribution



Monte Carlo

- Monte Carlo is a **computer program** (MC code) that **simulates** the transport of millions of photons and particles through the matter.
- It uses fundamental laws of physics to determine the **probability of distribution of interactions**.



- Larger the number of particles to be simulated (Histories) greater is the accuracy of prediction.
- But this increases computational time. Hence only a small randomly selected sample is simulated.
- This predicts the average behavior of all particles in the beam


Types of MC codes

- Electron Gamma shower version4 (EGS 4)
- PENELOPE
- Monte Carlo N Particle (MCNP)
- PEREGRINE
- ETRAN/ITS





IMRT - Delivery - Static

 Converting Intensity Map to Leaf positions ('Translator')



Beam Intensity Map



3 MLC Segments





Head & Neck

Organ	Mean Dose	Max Dose	Median Dose	Volume based	
Parotid Gland	26Gy	NA	NA	50% vol<30Gy or 20cc of both glands<20Gy	
Eye/Retina	NA	50Gy	NA	NA	
Optic Chiasm	NA	54Gy	NA	NA	
Mandible	NA	70Gy	NA	<1% vol >70Gy	
Brainstem	NA	54Gy	NA	<1% vol >54Gy	
PRV Brainstem	NA	60Gy	NA	<1% vol>60Gy	
Spinal Cord	NA	45Gy	NA	<1% vol >45Gy	
PRV Spinal Cord	NA	50Gy	NA	<1% vol >50Gy	
Lacrimal Gland	30Gy	NA	NA		

Head & Neck

Organ	Mean Dose	Max Dose	Median Dose	Volume based
Lens	NA	5-10Gy	NA	NA
Optic Nerve	NA	54Gy	NA	NA



Lung

Organ	Mean Dose	Max Dose	Median Dose	Volume based	
Spinal Cord	NA	46Gy	NA	1% vol<48Gy	
PRV S C	NA	50Gy	NA	1% vol <50Gy	
Total Lung- PTV	NA	NA	NA	V _{20Gy} <40%(RT alone) V _{20Gy} <35%(CTRT) V _{20Gy} <20%(CTRT-Sx)	
Heart	NA	NA	NA	V _{50Gy} <50%	
Oesophagu s	34Gy	NA	NA	Length receiving 60Gy<16cm	
Brachial plexus	NA	66Gy	NA	None	

Liu et al; IJROBP 2004 Lee et al, IJROBP 2003

Gynecological Malignancies

Organ	Mean Dose	Max Dose	Median Dose	Volume based	
U Bladder	45-48Gy	50Gy	45-48Gy	50% vol<35Gy; 66% vol<40Gy	
Rectum	42-45Gy	50Gy	42-45Gy	50% vol<35Gy; 66% vol<40Gy	
Small bowel	NA	50Gy	NA	30% vol<35Gy; 50% vol,25Gy	
Femoral head	NA	50Gy	NA	50% vol<40Gy	
Bone marrow	NA	NA	NA	V10 <90%; V20<75%	
Mundt et al; IJROBP 2003					

Prostate

Organ	Mean Dose	Max Dose	Median Dose	Volume based	
				V ₈₀ <15%	
Lirinary	15-18Gv	50Gv	15-	V ₇₅ <25%	
Bladder	43-48Gy 48Gy	30Gy	40-	V ₇₀ <35%	
	-			V ₆₅ <50%	
				V ₇₅ <15%	
Poctum	12-15Cv	5000	12-	V ₇₀ <25%	
Neclum	42-430y 45Gy	50Gy	72-	V ₆₅ <35%	
				V ₆₀ <50%	
Small bowel	NA	50Gy	NA	V ₄₅ <150cc	
				1	
		(RTOG	9406; IJROBP	2002)	
	and the second				

Prostate

Volume	Target	Absolute constraints	Relative constraints
CTV1	Prostate, prox SV	D _{100%} ≥100% pres dose	None
PTV1	CTV1+8mm except 5mm posteriorly	D _{95%} ≥100% pres dose D _{max} <17% pres dose V _{<65Gy} <1%	
PTV2	Distal SV+8mm	D _{95%} ≥100% pres dose	None
PTV3	LN+8mm	D _{95%} ≥100% pres dose	None
Rectum	From sigmoid flexure to ischial tuberosity	V _{<65Gy} <17% V _{<40Gy} <35%	90% isodose line encompasses no more than half width on any axial cut, 50% isodose line does not encompass full rectum width
Bladder	Partially filled entire bladder	V _{<65Gy} <25% V _{<40Gy} <50%	None
Femoral heads	Right and left femoral heads between trochanters	V _{50Gy} <10% for each (FCCC, Philadelphia, US)	None

Plan evaluation

- Dose statistic spreadsheet
 - To assess whether the plan acceptance criteria are met
- Dose- volume histogram(Quantitative)
 - To evaluate fraction of the defined volumes receiving high and low doses
- Slice by slice evaluation(Qualitative)
 - Dose conformity
 - Hot and cold spots

Qualitative evaluation

Isodose and dose colour wash display



Quantitative evaluation

Cumulative DVH

- Plot of entire volume of anatomical structure with specified dose or higher dose.
- Precision of DVH depends upon density of the sampling grid used.
 Coarse grid: Uncertain dose information
 Fine grid: Large computational time.
- Highlights hot and cold volumes at a glance.



Patient-Specific QA

- Comparison of the absorbed-dose distribution in a phantom with that calculated by the treatment planning computer for the same irradiation condition
- Measurement of the intensity pattern from individual beams for a specific patient.
- Measurement of the intensity pattern from individual beams for a specific patient.
- Measurements of absorbed dose in phantom of the beam-intensity pattern planned for a specific patient

Film and Ion Chamber QA



PTW OCTAVIUS[®] II







Detector size:

Detector spacing:

Max. field size: Max. measurement points: Reproducibility: Resolution: Measurement range: 0.5 cm x 0.5 cm x 0.5 cm (0.125 cm³) 10 mm center-to-center, 5 mm edge-to-edge 27 x 27 cm² 2916 (four measurements) $\leq \pm 0.5\%$ 1 mGy or 1 mGy/min (0.5 ... 45) Gy/min

Gamma Value





Gamma 2D - Parameters

3.0 mm Distance- To- Agreement
3.0 % Dose Difference with ref. to Max. dose of measured data set
Use increased tolerance of 5.0 % Dose Diff. for values below 0.1 Gy (or AU)
Suppress doses below 2.0 % of max. dose of measured data set

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Statistics

Number of Dose Points	729
Evaluated Dose Points	729 (100.0 %)
Passed	728 (99.9 %)
Failed	1 (0.1 %)
Result	99.9 % (Green)

Cottinge

Treatment Delivery

- Patient alignment verification using portal imaging is necessary
- Treatments may be delivered remotely or automatically under computer control







Imaging for treatment verification

- 1980's Port film
- 1990's Emergence of MV portal imagers
 - In-room ultrasound localization
 - Marker-based localization
 - Fluoroscopic tracking
- 2000's
- Flat panel imaging (EPID)
- KV digital imaging
- CT on rail
- KV-CBCT
- MV-CBCT

Goal and Clinical benefit

- To improve the accuracy of the radiation field placement
- To reduce the exposure of healthy tissue during radiation treatment



Tumor Motion During Respiration



Adaptive Radiotherapy

The clinical benefit for the patient is the ability to monitor and adapt to changes that may occur during the course of radiation treatment

Adaptive radiotherapy (cont.)

The courses of inaccuracies may include :

- Tumor shrinkage during the course of treatment
- Patient loss weight during the course of treatment
- Increase hypoxia during the course of treatment



Adaptive radiotherapy (cont.)

Allows us to correct for :

- Set up errors
- Inter-fraction organ motion : Inaccurate set up because of organ changes in each fraction
- Intra-fraction motion : Organ motion during treatment



Adaptive radiotherapy

Adaptive

Gating

- Set up errors
- Inter-fraction organ motion
- Intra-fraction motion

IGRT

<u>Two-dimensional</u> (2D) IGRT would include :

- Matching planar kilovoltage (kV) radiographs <u>fluoroscopy</u>
- CBCT with two orthogonal images
- megavoltage (MV) images with digital reconstructed radiographs (DRRs) from the planning CT.

IGRT

<u>Three-dimensional</u> (3D) IGRT would include :

- localization of a <u>cone-beam computed tomography</u> (CBCT)
- <u>computed tomography</u> (CT) data set from planning

Image-Guided RT Technologies

Ultrasound BAT SonArray I-Beam Restitu Video-Based Video Subtraction Photogrammetry AlignRT Real-Time Video-Guided IMRT

Related Technologies RPM gating/4DCT Optical-guided Approaches Planar X-Ray EPID CyberKnife Novalis RTRT Gantry-Mounted Protoype Tohoku, IRIS Commercial Varian OBI Elekta Synergy

Volumetric

In-Room CT FOCAL, MSKCC CT-on-Rails Primaton Varian ExaCT Tomotherapy MV Cone Beam CT Siemens kV Cone Beam CT Mobile C-arm Varian OBI Elekta Synergy Siemens In-Line

VOLUMETRIC (3D) IGRT



Siemens CTVision[™]



Varian Trilogy OBI®



Novalis Tx[™]



Siemens Artiste™ KVision



TomoTherapy® (HiART)



Elekta Synergy™ VolumeView



Elekta Axesse™





IGRT workflow ...



Patient positioned on the table in Tx. Position



Acquire scan using OBI



3D image fusion



Treatment Execution



Apply offset



Automatic table offset calculation



CTVision clinical case – Head & Neck



Adapted dose distribution after resorption of air and weight loss 2a and 2b

"

M.W. Münter MD, A. Jensen, MSc, P. Huber, MD, PhD The German Cancer Research Center Heidelberg, Germany


STEREOTACTIC RADIOSURGERY



STEREOTACTIC RADIOSURGERY

- "Stereo" Greek: Solid or 3dimensional
- "tact" Latin: to touch
- Stereotactic : 3 dimensional arrangement to touch
- Stereotactic Radiosurgery :
 - Technique of delivering high dose radiation to a specific target while delivering minimal dose to surrounding tissue



History of SRS

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Year	Author	Location	Event
1982	Betti <u>Colombo</u>	Buenos Aires Vicenza	Independent development of a system adapting LINACs for radiosurgery
1986	Lutz/ Winston	JCRT	Development of LINAC based SRS based on common stereotactic frame
1987	Lundsford	Pittsburgh	First Gammaknife installed in the US
1991	<u>Friedman/</u> <u>Bova</u>	Florida	Development of a more reliable technique for highly conformal radiosurgery
1991	Lax Blomgren	Karolinska	First to propose extending SRS outside of the skull
1992	Loeffler/ Alexander	Boston	First commercially built dedicated SRS LINAC (Varian-SRS)
1993	Laing	Boston	Gill-Thomas-Cosman relocatable frame

History of SRS

Year	Author	Location	Event
1994	Lax Blomgren	Karolinska	Stereotactic treatments of abdominal tumors (1994)
1994	Adler	Stanford	First clinical use of prototype of Cyberknife
1995	<u>Hamilton</u> Lulu	Arizona	First report of SBRT case in North America
2000	Murphy	Stanford	Introduces image-guided radiotherapy
2003	Le/Whyte Timmerman	Stanford Indiana	Lung tumor SBRT
2004	Fuss Salter	San Antonio	SBRT with tomotherapy

Radiosurgery - Definition

 Conformity describes how well the prescription dose is fitted to the target volume



High conformity, low selectivity

 Selectivity also takes irradiation to normal tissue into account



High conformity, high selectivity

Radiosurgery - Definition



Stereotactic radiosurgery and radiotherapy



GAMMA KNIFE

- The gamma knife device contains 201 <u>cobalt-60</u> sources of approximately 30 <u>curies</u> each
- It is placed in a circular array in a heavily <u>shielded</u> assembly.
- The device aims <u>gamma radiation</u> through a target point in the patient's brain.
- The patient wears a <u>specialized helmet</u> that is surgically fixed to their skull so that the brain tumor remains stationary at target point of the gamma rays.
 - Therefore it is also known as the <u>stereotactic</u> surgery.



Gamma knife radiosurgery flowchart

. Frame fixation



3. Treatment planning

2. Diagnostic imaging



4. Treatment





Stereotactic Radiosurgery

1982: Modified Linear Accelerator



Stereotactic Radiosurgery

SRS Frame Placement



STEROTACTIC RADIATION THERAPY SRT



Fractionated Stereotactic Radiation Therapy

Multiple fraction with stereotactic frame



Fractionated Stereotactic Radiation Therapy



Stereo tactic Body Radio Therapy



Stereo tactic Body Radio Therapy

Use of external beams to treat lesions of the body with "surgical" doses and high precision tumor identification and relocalization employing "stereotactic" image guidance or implanted fiducials.



SBRT REQUIRES:

- Higher confidence in tumor targeting
- Reliable mechanisms for generating focused, sharply delineated dose distributions
- Reliable accurate patient positioning accounting for target motion related to time dependent organ movement

SBRT: who started it?



TABLE 2	Anatomic Distribution of 1965 Tumors		
	That Have Been Treated with		
	Stereotactic Body Radiation Therapy at		
	the Karolinska Hospital from 1991 to		
	2003.		

Organ	No. Tumors	
Lungs	997	
Mediastinum	78	
Liver	484	
Pancreas	149	
Suprarenal glands	30	
Abdomen	118	
Skeleton	25	
Miscellaneous⁵	46	

Mainly kidneys and para-aortic regions.
Pelvic area, muscles, and so forth.

Answer: Blomgren and Lax, Karolinska Institute, Stockholm, Sweden

SBRT: who started it?

Prelude to a New Therapeutic Paradigm: The Clinical Transition from Intracranial to Extracranial Stereotactic Radiation Therapy

Ingmar Lax and Henric Blomgren



FIGURE 1. The left panel shows a schematic drawing of intracranial stereotactic radiosurgery with the Gamma Knife (Elekta, Norcross, GA). The stereotactic frame is fixed with screws into the skull. The right panel shows a schematic drawing of extracranial stereotactic radiation therapy with linear accelerator. The patient is fixed in the stereotactic body frame.

Conventional vs SBRT



FIGURE 2. Illustration of coordinate systems used in conventional radiotherapy (left) and stereotactic body radiation therapy (right).

Linear Accelerators with features especially suitable for SBRT





COLLIMATORS

- Twelve Secondary Collimators (5mm dia. to 60 mm dia.)
- Variable Aperture collimator -Iris



TRACKING SYSTEM

- 6D skull tracking system
- X-sight Spine tracking
- Fiducial tracking
- Synchrony Respiratory
 tracking

6D SKULL TRACKING

- Used for cranial lesions down to C3
- Uses bony anatomy from DRRs as reference
- Position calculated in 6 degrees (Transverse and rotational)
- Fast and accurate (better than 0.5 mm accuracy)



Fidicial Tracking System

- Gold Seed fidicial :
 - Diameter : 0.7 to 1.2mm
 - Length : 3 mm to 6 mm
- Minimum one fidicial is need to track translation error
- Minimum three fidicial is need to track both translation and rotational error



Fidicial Tracking System



Xsight[™] Spine Tracking System

- Automatically locates and tracks tumors along the spine
- Eliminates the need for surgical implantation
- Utilizes the bony anatomy of the spine:
 - Cervical
 - Thoracic
 - Lumbar
 - Sacrum



TREATMENT PLANNING PROCEDURE



Treatment Planning – Image fusion



Treatment Planning – Contouring



Treatment Planning – Alignment (6D Skull)



Treatment Planning – Alignment (Xsight Spine)



Treatment Planning – Alignment (Fidicial)


Treatment Process -Treatment planning parameter selection

- Collimator size (40% to 60% target area)
- Optimization technique
 - Isocentric / isocentric conformal
 - Conformal
 - Simplex
 - Iterative
- Target and critical structure constraints
- Tuning and avoidance structures
- Minimum / maximum MU

Treatment Process -Treatment execution

• Final Plan Export to CK Control console



Planed at our site.....



Flattening Filter Free Beam



Flattening Filter Free Beam



- Dose Rate High (~ 2400 MU/min)
- Reduced scatter , leaf transmission and radiation head leakage
- Reduced peripheral exposure



- Without FF : Forward peaked bremsstrahlung spectrum
- To compensate for this effect Flattening Filter (FF) has been introduced

Due to this :

- Dose rate substantially affected(~ 600MU/min)
- A major source of head scatter

Flattening Filter Free Beam

Removal of the flattening filter from the LINAC Head..



FFF BEAM PROFILE..



6X-FF

10X-FF



TRUE BEAM

- Multi-Energy: 13 Carousel Positions available
- 4 Flattened Photon Energies: 6, 8, 10 & 15 MV
 - From low dose rates through 600 MU/min
- 2 High Intensity Mode Energies:
 6X FFF, 10X FFF (Flattening Filter Free, 2400 MU/min)
- 8 electron energies: many foils, 22e (max)



SBRT liver with TB: 25Gy x 3; 10FFF; DR 2400.



Abdominal Mets SBRT. 10XFFF, DR:2400. 6x7.5 Gy





1 isoc, 1 arcs Jaws tracking MU: 1697 BOT: 60 sec





Kidneys mean dose = 1.5 Gy Spine: max dose = 7.5 Gy

Medica

SBRT: 3.5Gyx10;6FFF;DR 1200.





Rectum mean dose = 9.9 Gy Femoral heads mean dose = 1.6 Gy





1 isoc, 1 arcs Jaws tracking MU: 1065 BOT: 66 s

