STEREOTACTIC BODY RADIOTHERAPY

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Definition

"SBRT is the term applied in USA by ASTRO for the management and delivery of Image Guided high dose Radiation Therapy with tumor ablative intent within a course of treatment that does not exceed 5 fractions."

Conventional RT vs. SBRT

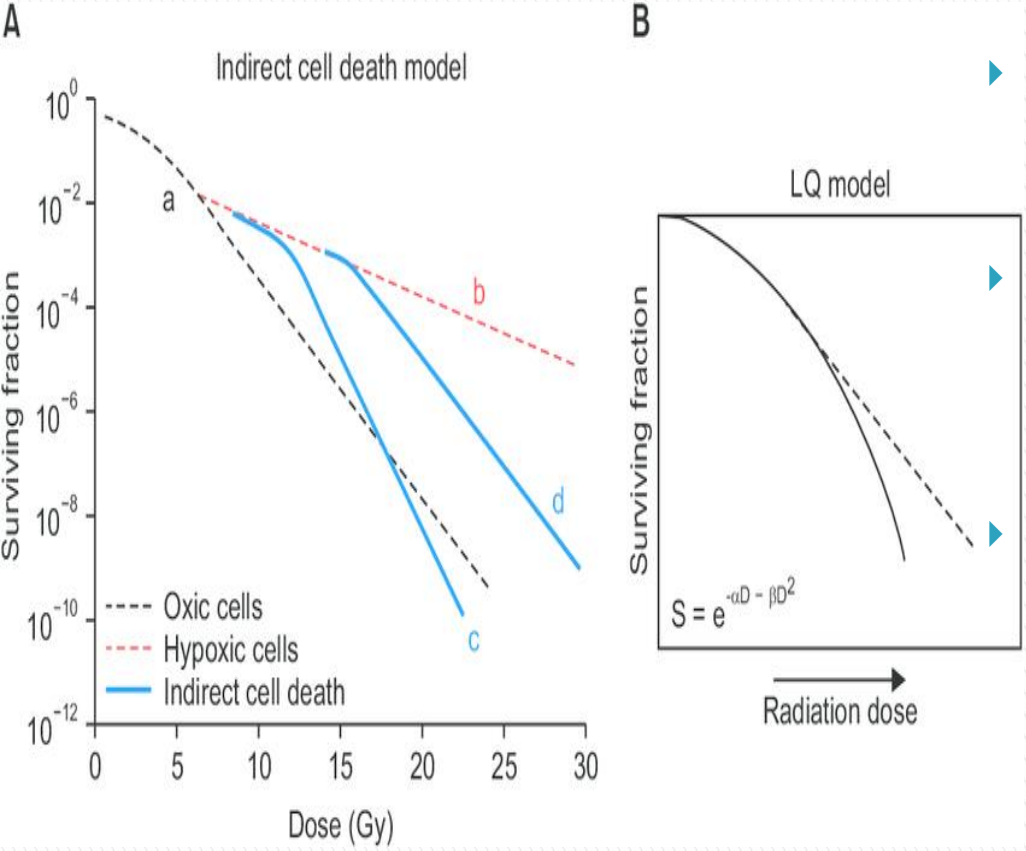
Characteristic	Conventional RT	SBRT
Dose / Fraction	1.8 – 3 Gy	6 – 30 Gy
No. of Fractions	10 – 30	1-5
Target definition	CTV / PTV gross disease + clinical extension: tumor may not have a sharp boundary.	GTV / CTV / ITV/ PTV well-defined tumors: GTV=CTV
Margin	Centimeters	Millimeters

Although SBRT employs similar basic principles as in conventional modalities including IMRT and IGRT, its extreme hypo fractionated treatment delivery demands the utmost consideration for safety!

Radiobiology

- Although an increasing number of cancer patients are treated with SBRT and SRS in recent years, the biological mechanisms of these new modalities have been unclear.
- A simple calculation based on the radiobiological principles for the conventional multi-fractionated RT clearly suggests that tumor cell death caused by DNA damages by direct effect of radiation alone **cannot account for the high efficacy of SBRT and SRS.**
- Evidence now indicates that SBRT and SRS with doses higher than about 10 Gy per fraction induces severe vascular damages in tumors, which then cause secondary and additional tumor cell death.
- The ensuing degradation of tumor cells would then release massive tumor-specific antigens, thereby elevating anti-tumor immune response leading to suppression of recurrence of tumors and metastasis.
- **The role of 4 Rs and the LQ model is limited in SBRT and SRS.**

Hypothetical radiation survival curve of tumor cells in vivo assuming about 10% of the tumor cells are radio biologically hypoxic.



The 'a' corresponds the radiation-induced death of oxic cells

'b' indicates the death of hypoxic cells assuming that radiation-induced cell death is due only to direct damage in DNA/chromosomes.

'c' and 'd' show indirect and additional cell death due to vascular damages at high radiation doses.

(B) The dotted line indicates decline in cell survival when radiation-induced cell death is linearly related to radiation dose.

Solid line is the linear-quadratic (LQ) survival curve which bends downward at high radiation dose indicating that the LQ model overestimates cell death at high radiation doses.

Methods Of Cell Kill in SBRT

- DNA damage ▪
- Anti Angiogenesis ▪
- Endothelial cell Apoptosis

BIOLOGICAL AND ONCOLOGICAL RATIONALE OF SBRT

- The appeal of SBRT is based on the nonlinear relation between radiation dose and cytotoxic effect.
- One or a few large individual doses of radiation therapy have substantially more cell-killing effect than the same dose of radiation given in smaller individual dose
- Beyond its uses as primary therapy for selected early-stage cancers,
- SBRT has also been used as a noninvasive and efficient means of eradicating discrete metastatic tumors

- A consideration –emerged in recent years
- Possibility that high dose/#–radiation therapy influences immune system responses in a manner that can be exploited for favorable therapeutic effect.
- Preclinical studies have demonstrated that high-dose/# ionizing radiation can induce antigen presentation within the tumor stroma.
- Antibody-mediated induction of T cell activity can be combined with high dose/# ionizing radiation to enhance not only the effect on the irradiated tumor but also to create an abscopal effect whereby tumor implants remote from the irradiated site regress.
- These suggest ideas for new investigations into the combination of SBRT and immuno modulatory agents for patients with metastatic disease.

SBRT Hypothesis

- High dose fractionated RT may provide high probability of Local control in case of Inoperable & Medically inoperability
- Improved therapeutic ratio
- High focused RT provide similar control where limited surgical care is standard of care.

Rationale

- ▪ Conceptual theories of cancer growth and numerous lines of evidence behind use of SBRT for metastatic lesions are
- (a) The Empiric Or Phenomenological,
- (B) The Patterns-of-failure Concept,
- (C) The Theory Of Oligo- metastases,
- (D) A Lethal Burden Variation Of The Norton-simon Hypothesis
- (E) Immunological Enhancement

Simon –Norton Hypothesis

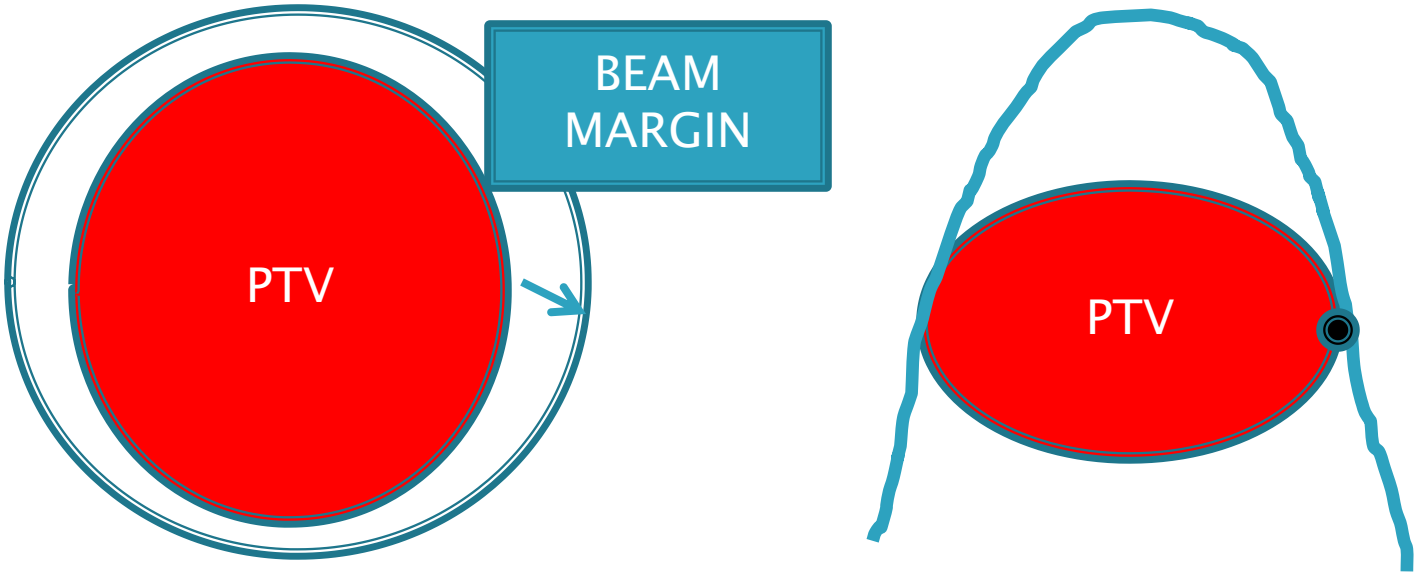
- Tenets of this hypothesis has two goals
- 1) to reduce the tumor burden in such a way that the remaining cancer cells within in the body enters into a state of higher growth fraction thus become more susceptible to cytotoxic treatment.
- 2) to prevent or delay as long as possible the lethal tumor burden that is fatal to patient

ASTRO-ACR GUIDELINES

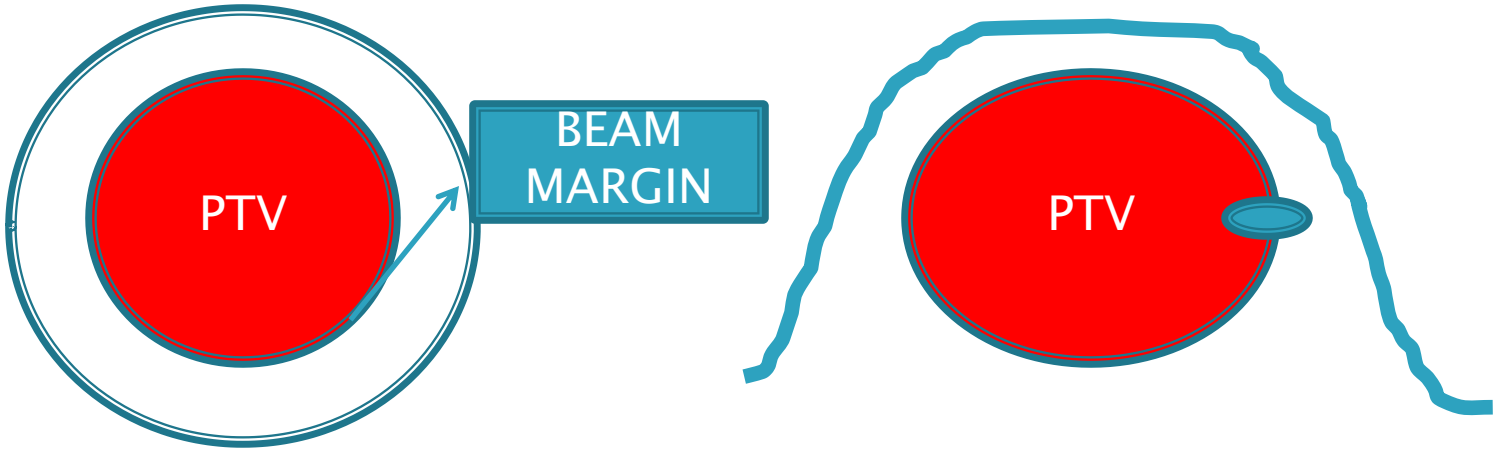
- Qualified personnel:
  - Board-certified radiation oncologist
  - Qualified medical physicist
  - Licensed radiation therapist
  - Other support staff as indicated (dosimetrists, oncology nurses, and so forth);
- Ongoing machine quality assurance program;
- Documentation in accordance with the *ACR Practice Guideline for Communication: Radiation Oncology*;
- Quality control of treatment accessories;
- Quality control of planning and treatment images;
- Quality control of treatment planning system;
- Simulation and treatment systems that account for systematic and random errors associated with setup and target motion in a manner that is based on actual measurement of organ motion and setup uncertainty.

- In general to achieve a tightly focused high-dose distribution within the PTV and rapid dose falloff outside the PTV, a combination of multiple (often 10 or more) noncoplanar beams or multiple arcs are required. Intensity modulation across the individual beams or arc segments can be incorporated within SBRT.

- If beam margin is much less than beam penumbra (0–2 mm) → Inhomogeneous PTV dose, Maximum dose ~ 125% or more of PD. Dose fall off outside PTV is fast



- If beam margin is close to beam penumbra (5-6 mm)→ Homogeneous PTV dose, Maximum dose about 110% of Prescription Dose (PD).
- Dose fall off outside PTV is slow



Stereotactic Body Radiation Therapy (SBRT)

- Fractional dose >5Gy
- Range: 5 Gy to 34 Gy per fraction ·
- Number of fractions < 5
- Range 1 -5
- Safe delivery is of utmost importance due to high fractional dose and small number of fractions.

The Basics of Treatment Planning for SBRT

- The goal of SBRT treatment is to “ablate” tissues within the PTV,(these tissues were not considered at risk for complications).
- Dose in homogeneity inside the PTV was considered acceptable (potentially advantageous) not considered a priority in plan design.
- Maximum point dose up to 160% of Prescription Dose is common for SBRT plans
- The main objective of the plan is to minimize the volume of those normal tissues outside PTV receiving high dose per fraction

SBRT PHYSICS AND TECHNOLOGY

- 1. CT simulation: Assess tumor motion ▪
- 2. Immobilization: Minimize motion, breathing effects ▪
- 3. Planning: Small field dosimetry considerations ▪
- 4. Repositioning: High precision patient set-up: Fiducial systems, IR/LED Active and Passive markers, US, Video ▪
- 5. Relocalization: Identify tumor location in the treatment field: *
- MV/ KV Xray, Implanted markers and/or set-up fiducials *
- Motion tracking and gating systems *
- Real-time tumor tracking systems with implanted markers ▪
- 6. Treatment delivery techniques ▪ Adapted conventional systems ▪ Specialized SRT: Novalis, Cyberknife, True- Beam

SBRT Requires

- *Secure immobilization*
- *Stereotactic body frame (?) Reliable IGRT friendly immobilization*
- *Well defined tissue (tumor and normal) delineation*
- *Multi-modality, motion compensated imaging*
- *Reliable mechanisms for generating focused, sharply*
- *delineated dose distributions*
- *Non-opposing, well collimated co-planar and non-coplanar beamarrangements*
- *3DCRT or IMRT /VMAT techniques and optimal beam margins*
- *Reliable mechanisms to control/compensate organ motion*
- *Breath hold techniques or gating*
- *Accurate and precise targeting*
- *Image guided targeting*
- *Few fractions, high dose*

SBRT CT simulation

- For upper thoracic regions, both arms (elbows) should be over the patient's head and included in the CT scan so that clearance of beams can be visualized during planning.
- •Scan 15 cm beyond field borders (sometimes non-coplanar beams are needed).
- •For spine cases, include sacrum for lower spine or include C1 for upper spine so that vertebrae can be easily identified

Treatment Planning for SBRT

- Ablative intent for SBRT
- Dose inhomogeneity inside the PTV is acceptable
- Maximum point dose up to 160% of Prescription Dose within PTV is common for SBRT plans.
- Minimize the volume of normal tissue irradiation outside of the PTV
- MUST respect all normal tissue dose limits

SBRT Treatment Planning Guidelines:(RTOG 0813 &0915 lung protocols)

- **Maximum Dose: normalized to 100%, must be within PTV**
- **Prescription Isodose: must be ≥ 60% and < 90% of the maximum dose**
- **• PTV Coverage:**
  V 100% PD = 95%
  V 90% PD > 99%
- **High Dose Spillage**: cumulative volume of all tissue outside the PTV receiving a dose > 105% of prescription dose should be no more than 15% of the PTV volume
- **Intermediate Dose Spillage**: falloff gradient beyond the PTV extending intonormal tissue structures must be rapid in all directions
- **• All normal tissue dose limits need to be respected**

Spectrum of potential applications of SBRT

- Intensified treatment to a primary cancerStage I
- lung cancer
- Primary HCC
- **Pancreas cancer**
- Prostate cancer

- Palliation/control for challenging sites recurrence
- Spinal
- Retroperitoneal
- Previously irradiated volumes

- **Adjuvant systemic cytoreductive therapy"Radical" treatment for isolated liver, lung, spine, and other mets**

University of Chicago SBRT Experiences

- • Oligometastases trial (2004-2010)
- • Phase I Trial
- • 5 sites, 3 x 8Gy → 18Gy
- • Large Metastases (2005 – now)
- • 5 Gy x 10
- • Lung
- • Primary Tumors (<4.5 cm):
- • 12 Gy or 10 Gy x5
- • Liver
- • Mets: 10 Gy x 5 or 20 Gy x3
- • HCC: 30-50 Gy in 5 fx (Veff)
- • Spinal Mets
- • 16 Gy-18 Gy: Single fraction
- • 8 Gy x 3

Benefits of Stereotactic Ablative Radiotherapy

- Outpatient
- 20-60 Minutes Per Treatment
- Entire course of Rx in1-2 weeks
- No Sedation or Anesthesia (painless)

1-5 Treatments qd or qod

Immediate Return To Activities

SBRT Lung/Liver/Abdominal Cases

- 4DCT simulation must be done first to access tumor motion range
- •Gating will be considered only if motion > 0.5cm, and the patient has a regular, reproducible breathing pattern; alternatively, an ITV can be created.
- •For gating cases, Blue BAGTM without vacuum suction is used as immobilization device.
- •Abdominal Belt Compression system can be used for some patients
- •Fiducials necessary for Liver/Abdominal Cases: no other way to visualize tumor. CBCT image quality, FOV limitation for lateral tumors.
- •If no fiducials for Lung cases, Fluoro on the machine must be done before simulation to verify visualization of tumor

CONSTRAINTS

- Normal Liver: defined as Liver mi us GTV
- >700cc Liver volume must be outside PTV
- Mean Liver GTV dose- 18 Gy
- Heart-maximum dose is 40Gy to 0.1cc
- Kidney-If only one functional kidney or one kidney is Irradiated with 12 Gy: > 80% of the oppsoite kidney must receive <12 Gy& V6 <10%.
- Ideally 2/3 of the combined kidney vol. must receive <15 Gy
- Spinal cord: max dose is 27 Gyto 0.1 cc

- SBRT Registry: Liver
- If lesions > 2cm from Porta Hepatis/Bile Duct: Three Fractions 20Gy x 3
- If lesions ≤ 2cm from Porta Hepatis/Bile Duct: Five Fractions 10Gy x 5
- Liver minus-GTV: >700mL receive < 10%
  Colon/Rectum: Maximal dose 34 Gy to 0.5 cc
  Spinal Cord: Maximal point dose is 18 Gy (6 Gy per fraction)
- Skin: Maximal point dose is 24 Gy (8 Gy per fraction)

- SBRT IN FEW ABDOMINAL MALIGNANCIES

SBRT Lung/Liver/Abdominal Cases

- If no fiducials, create fluorobeam aperture that hugs GTV.
- ·If there is fiducials, create fluorobeam aperture that use fiducialsas corners.
- ·CBCT alignment with GTV, bony landmark secondary but should be less than 1cm discrepancy. Otherwise, reposition patient.
- ·CBCT sometimes do not align well with average simCT due to breathing variation
- ·Fluoro to verify positioning after CBCT.
- ·Fluoro between fields to monitor setup consiste

SBRT Lung/Liver/Abdominal Cases

- If non-gating, may consider one or both arms on the side. Non-coplanar beams could be used to compensate for lateral beams. If gating is used, only coplanar beams can be used for some machines, arms on the side could further limits beams.
- •VMAT is a good option (can not be combined with gating for many machines)
- •Gating + fixed beam IMRT or EDW is not advisable (takes way too long to deliver), use FIF instead if you must.
- •Beam arrangement should consider collision possibility for lateral tumors. Keep beams /arcs on the ipsilateralside.
- SBRT Lung/Liver/Abdominal Cases

Stereotactic body radiotherapy (SBRT) with or without surgery for primary and metastatic liver tumors

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Abstract

Objectives: We report single center experience on the outcome and toxicity of SBRT alone or in combination with surgery for inoperable primary and metastatic liver tumors between 2007 and 2014.

Patients and methods: Patients with 1–4 hepatic lesions and tumor diameter ≤9 cm received SBRT at 46.8Gy ± 3.7 in 4–6 fractions. The primary end point was local control with at least 6 months of radiographic followup, and secondary end points were toxicity and survival.

Results: Eighty-seven assessable patients (114 lesions) completed liver SBRT for hepatoma (39) or isolated metastases (48) with a median followup of 20.3 months (range 1.9–64.1). Fourteen patients underwent liver transplant with SBRT as a bridging treatment or for tumor downsizing. Eight patients completed hepatic resections in combination with planned SBRT for unresectable tumors. Two-year local control was 96% for hepatoma and 93.8% for metastases; it was 100% for lesions ≤4 cm. Two-year overall survival was 82.3% (hepatoma) and 64.3% (metastases). No incidence of grade >2 treatment toxicity was observed.

Conclusion: In this retrospective analysis we demonstrate that liver SBRT alone or in combination with surgery is safe and effective for the treatment of isolated inoperable hepatic malignancies and provides excellent local control rates.

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Challenges in Targeting Liver Tumors

- Limited visualization of the target
- Liver deformation with respiration
- Changes in GI organ luminal filling
- Critical structures (stomach) may change in shape and position between planning and treatment
- Inter fraction target displacement with respect to bony anatomy

Abdominal compression

- Abdominal belt with inflatable bladder
- Inflation: 15-40 mmHg

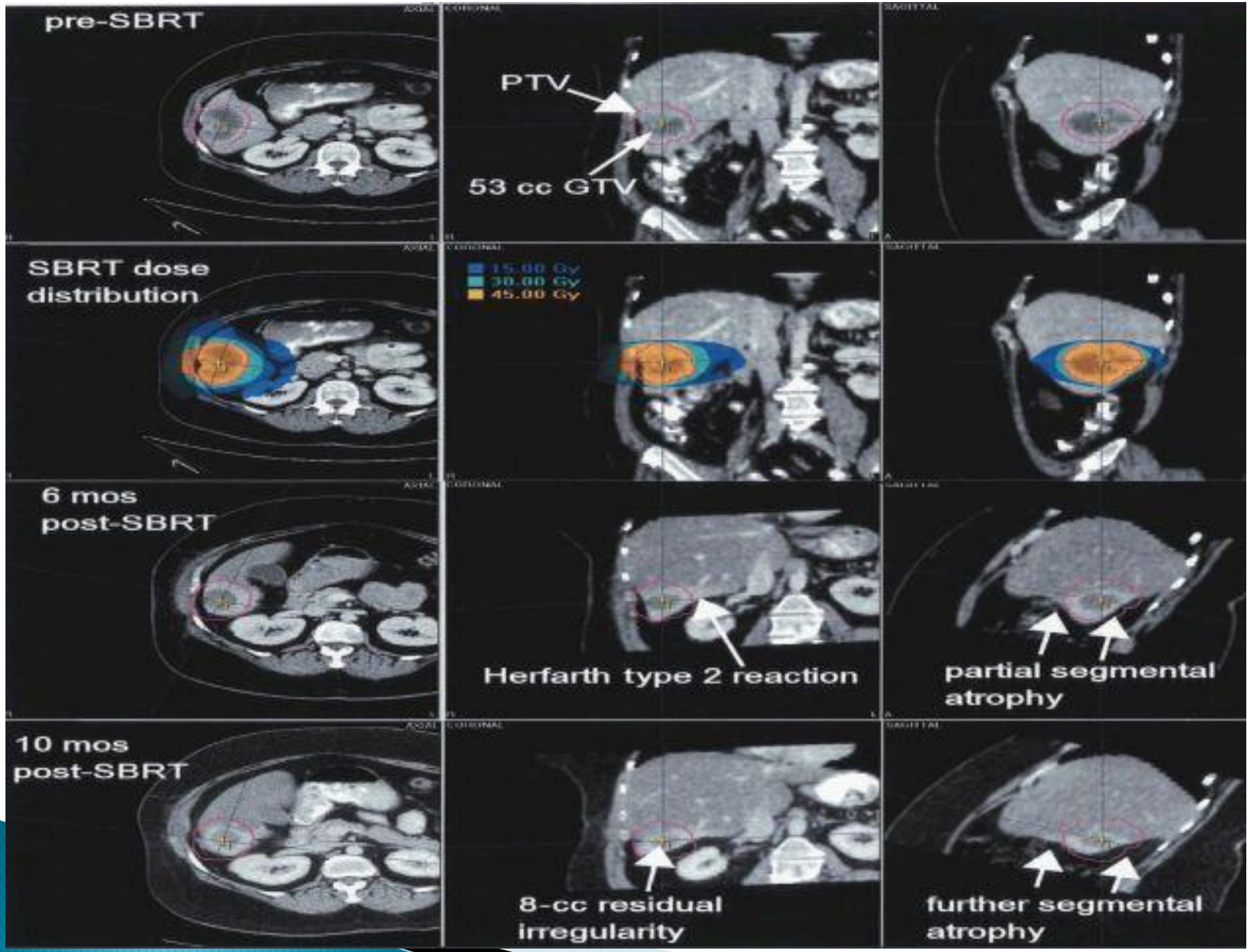
First Liver SBRT Experience

- 50 patients treated to 75 lesions with SBRT for primary and metastatic liver tumors ▪
- 15 to 45 Gy, 1-5 fractions ▪
- Mean follow-up of 12 months ▪ 30% of tumors demonstrated growth arrest, 40% were reduced in size, and 32% disappeared by imaging studies ▪
- 4 local failures (5.3%) ▪
- Mean survival time was 13.4 months Blomgren, et. al., J Radio-surgery 1998

TABLE 17.1 STEREOTACTIC BODY RADIATION THERAPY FOR LIVER METASTASES

Institution (Ref.)	*Patients/Lesions*	*SBRT Dose and Fractionation*	*Results*
Heidelberg (44)	37/60	11–21 Gy × 1	18 months LC: Low dose (<16): 0% High dose (>16): 81%
Würzburg (45)	39/51	7 Gy × 4 10 Gy × 3 12.5 Gy × 3 26 Gy × 1	2 year LC: Low dose (28–30): 58% High dose (others): 82%
Aarhus-Copenhagen (46)	44/not stated	10 Gy × 3	2 year LC: 79% All pts CRC 3 ulcers with intestinal dose >30 Gy
Erasmus (47)	17/34	10 Gy × 3 12.5 Gy × 3	54% 15 pts CRC; 1 late portal hypertension in multiply treated patient
Colorado/multi-institutional (48)	47/63	12–20 Gy × 3	2-year LC: ≤3 cm: 100% >3 cm: 75%
Princess Margaret Hospital (49)	68/141	Variable, NTCP-based Median 7 Gy × 6	1-year LC: 71% Better for higher dose, smaller volume
Stanford (50)	19/35	18–30 Gy × 1	1-year LC: 77% Combined with 7 patients with primarily liver cancer; maximum tolerated dose not reached
University of Texas–Southwestern (51)	26/35	6–12 Gy × 5	2-year LC 56%, 89%, 100% for total dose 30, 50, 60 Gy, respectively

PTV, planning target volume; LC, local control; OS, overall survival; CRC, colorectal cancer; NTCP, normal tissue complication probability.


pre-SBRT
PTV
53 cc GTV
SBRT dose distribution
15.00 Gy
30.00 Gy
45.00 Gy
6 mos post-SBRT
Herfarth type 2 reaction
partial segmental atrophy
10 mos post-SBRT
8-cc residual irregularity
further segmental atrophy

PANCRAETIC CANCER

ELSEVIER

Seminars in
RADIATION
ONCOLOGY

Stereotactic Body Radiotherapy in the Treatment of Pancreatic Cancer

Nicholas Trakul, MD, PhD,* Albert C. Koong, MD, PhD,† and Daniel T. Chang, MD†

Most patients diagnosed with pancreatic cancer are unable to have a curative surgical resection. Chemoradiation is a standard of care treatment for patients with locally advanced unresectable disease, but local failure rates are high with conventionally fractionated radiotherapy. However, stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy offers an alternative type of radiation therapy, which allows for the delivery of high-dose, conformal radiation. The high doses and shorter overall treatment time with SBRT may provide advantages in local control, disease outcomes, quality of life, and cost-effectiveness, and further investigation is currently underway. Here, we review the technology behind SBRT for pancreatic malignancy and its future direction in the overall management of pancreatic cancer.
Semin Radiat Oncol 24:140-147

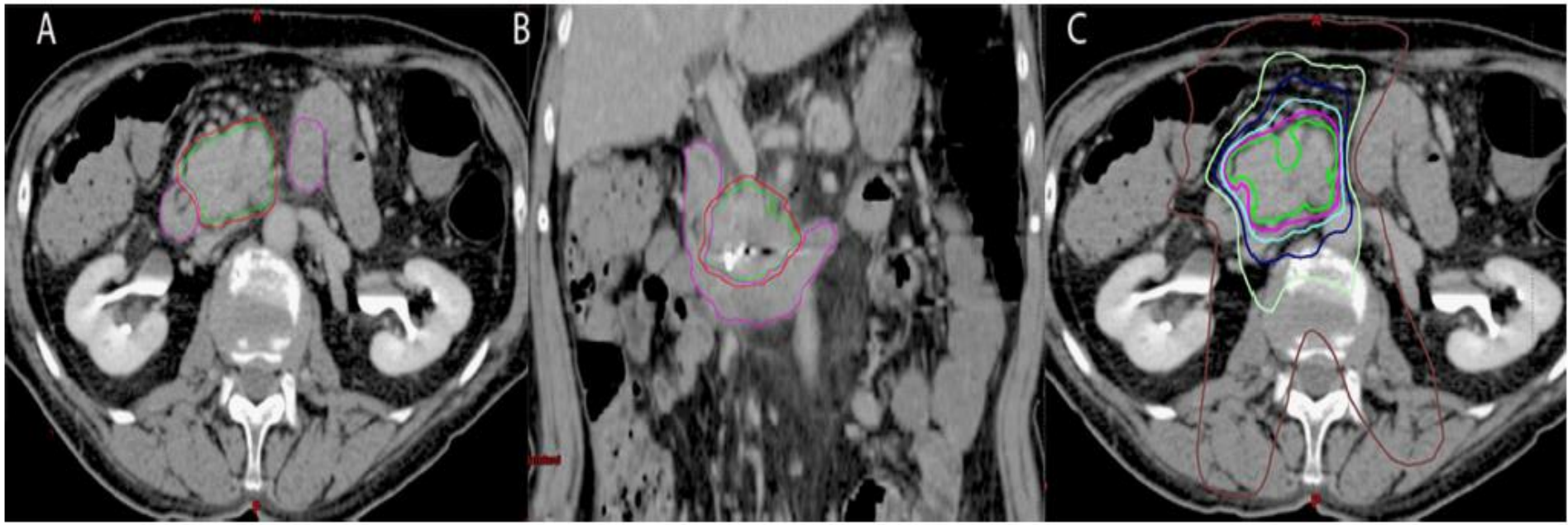


Figure Representative pancreatic SBRT plan: (A) axial view showing pancreatic tumor (GTV: green), a typical PTV (red), and the duodenum (magenta); (B) coronal view demonstrating tumor relationship with the duodenum; and (C) dose distribution for a plan treating to 33 Gy in 5 fractions. Isodose lines: green = 45 Gy; magenta = 40 Gy; cyan = 33 Gy; blue = 30 Gy; light green = 20 Gy; and brown = 10 Gy. Abbreviation: GTV, gross tumor volume. (Color version of figure is available online.)

Table Outcomes in Reported Studies of Pancreatic SBRT

References	Patients	Dose	Local Control (1 y Unless Specified)	Median Survival (mo)	Toxicity	Chemo
Koong et al[26]	15 LA or LR	15-25 Gy × 1	100%	11	33% Grades 1 and 2 0% ≥ Grade 3	None
Koong et al[27]	16 LA	25 Gy × 1 (boost)	94%	8.3	69% Grades 1 and 2 12.5% ≥ Grade 3	5-FU with EBRT prior to boost
Hoyer et al[34]	22 LA	15 Gy × 3	57%	5.4	79% ≥ Grade 2 4.5% Grade 4	
Schellenberg et al[28]	16 LA	25 Gy × 1	100%	11.4	19% Acute 47% Late	1 Cycle induction GEM + post-SBRT GEM
Didolkar et al[35]	85 LA or LR	5-10 Gy × 3	92%	18.6	22.3% ≥ Grade 3	Post-SBRT GEM
Mahadevan et al[30]	36 LA	8-12 Gy × 3	78%	14.3	33% Grades 1 and 2 8% Grade 3	Post-SBRT GEM
Polistina, et al[32]	23 LA	10 Gy × 3	82% 6 mo 50% 1 y	10.6	20% Grade 1 0% ≥ Grade 2	6 wk induction GEM
Mahadevan et al[31]	39 LA	8-12 Gy × 3	85%	20	41% Grades 1 and 2 0% ≥ Grade 3 (acute) 9% Grade 3 (late)	2 Cycles induction GEM
Rwigema et al[36]	71 LA, LR, RPM, and MD	24 Gy (med) × 1 (94%) 8-10 Gy × 2-3 (6%)	71.7% 6 mo 48.5% 1 y	10.3	39.5% Grades 1 and 2 4.2% Grade 3	90% Received chemo (various regimens)
Schellenberg et al[29]	20 LA	25 Gy × 1	94%	11.8	15% Grades 1 and 2 5% ≥ Grade 3	1 Cycle induction GEM + post-SBRT GEM
Goyal et al[37]	19 LA or LR	20-25 Gy × 1 8-10 Gy × 3	81%	14.4	11% Grades 1 and 2 16% Grade 3	68% Received chemo (5-FU or GEM based)
Lominska et al[40]	28 LA or LR	4-8 Gy × 3-5	86%	5.9	7% Grade 3 (late)	5-FU or GEM prior to SBRT
Gurka et al[33]	10 LA	5 Gy × 5	40%	12.2	0% ≥ Grade 3	1 cycle GEM prior, 6 cycles GEM total
Chuong et al[38]	73 BR or LA	5-10 Gy × 5	81%	16.4 BR 15 LA	5% Grade 3 (late)	3 cycles GTX

Abbreviations: BR, borderline resectable; 5-FU, 5-flourouracil; GEM, gemcitibine; GTX, gemcitibine, taxotere, and xeloda; LA, locally advanced; LR, locally recurrent; MD, metastatic disease; RPM, resected positive margins; SBRT, stereotactic body radiotherapy.

SBRT for Pancreatic Cancer

- •Advantages of SBRT over conventionally fractionated radiotherapy
- -1-2 weeks vs6 weeks of therapy
- -Greater dose conformality
- •Fewer acute complications
- -No delay in administration of systemic chemotherapy

- SBRT TRIALS IN PANCREATIC MALIGNANCY

Study	N	Prior EBRT	Regimen	Median OS Months	Toxicity
Koong, Phase I	15	2	15-25	11	33% grI-2/NR
Koong Phase II	16	16	45/25#+ 25/1 #	8.3	12%acGr.3/gr2 ulcers
Schellenburg	16	0	25/1#	11.4	6% ac,G3 13% late G3
Hoyer,		0	45 Gy/3 fx	5.7	18%severe GI toxicity
Mahadevan, 2010	36	0	24-36 Gy/3 fx	20	5%gr 3
Polistina, 2010	23	0	30 Gy/3 fx	10.6	0
Tozzi, 2013	30	0	45/6	11	0
Gurka 2013	11	0	25/5	12.2	0
Herman 2013	49	0	33/5	13.9	8% gr3

Phase II Study of Gemcitabine + SBRT

- **LOCALLY ADVANCED CA PANCREAS → GEMCITABINE → SBRT**
- **GEMCITABINE**

- 16 patients received 1-3 weeks of gemcitabine prior to SBRT
- •Median follow-up: 9.1 months
- •Median OS: 11.4 months, 2 year OS: 12.5%
- •Median TTP: 9 months
- -3 patients had LR by PET/CT
- -14/16 had DM as first site of progression
- **Locally Advanced**
- **Pancreatic CA**
- **25 Gy**
- **Gemcitabine**
- **Gemcitabine**
- SchellenbergD, Goodman K, *et al., IJROBP, 2008*

Acute complications

Grade	Complication	Prior Surgery	Therapy	Weeks post treatment
2	Gastritis and pain	CDJ-GJ	None	<6 wks
2	Gastritis and pain	Aborted Whipple	Medical	<6 wks
3	Ulcer, gastritis, pain	CDJ-GJ	Medical and J-tube	6 wks

*CDJ – Choledocojejunostomy

*GJ - Gastrojejunostomy

Schellenberg D, Goodman K, *et al.*, IJROBP, 2008

Late complication

Grade	Complication	Weeks After SBRT	Previous surgery	Tx received
2	Duodenal-Jejunal ulcer	29	CDJ-GJ	Medical management
2	Duodenal ulcer	22	CDJ-GJ	Medical management
2	Duodenal ulcer	26	CDJ-GJJ	Medical management
2	Gastric-Duodenal ulcer	32	None	Medical management
2	Duodenal ulcer	20	None	Medical management
3	Duodenal stricture requiring stent	46	None	Duodenal Stent
4	Duodenal ulcer & perforation requiring surgery	34	CDJ-GJ	Surgery

Schellenberg D, Goodman K, *et al.*, IJROBP, 2008

Duodenal Doses

Median time to duodenal toxicity: 6.2 mos

6-and 12-mo actuarial rates of toxicity: 11% and 29%

Variable*	Cutoff†	Incidence of Grade 2–4 duodenal toxicity (%)‡	Log-rank *p* value
V5			
	<25 cm^3	28	0.39
	≥25 cm^3	31	
V10			
	<16 cm^3	15	0.015
	≥16 cm^3	46	
V15			
	<9.1 cm^3	11	0.002
	≥9.1 cm^3	52	
V20			
	<3.3 cm^3	11	0.002
	≥3.3 cm^3	52	
V25			
	<0.21 cm^3	12	0.010
	≥0.21 cm^3	45	

* V5 refers to the volume of duodenum receiving 5 Gy.
† Cutoff refers to the median value.
‡ Actuarial incidence at 12 months.

Murphy J, *et al., IJROBP, 2012*

Danish SBRT Experience

- Phase II trial of SBRT (15 Gy x3) for locally advanced pancreatic cancer
- • 22 patients treated to tumor (GTV) and surrounding edema (CTV) + 5mm radial margin, 10 mm cranio-caudal margin (PTV)
- • Electa or Varian planning and delivery systems
- *Hoyer M, et al. , Radiother Oncol, 2005*

Median survival was 5.7 months

- 1 year OS 5%
- 79% progressed to ≥ Grade 2 toxicity within 14 days of SBRT

Performance status (PS) and toxicity grade at base-line and 14 days after treatment

	Base-line PS and grade					14 days after treatment PS and grade				
	0	1	2	3	4	0	1	2	3	4
Performance status[a]	6	12	3	1	0	3	5	8	2	0
Nausea[a]	15	5	2	0	0	4	3	7	4	0
Diarrhoea	15	5	0	2	0	12	3	1	2	0
Pain[a]	7	3	9	3	0	2	3	4	8	0
Analgesic consumption	8	0	2	3	9	2	2	1	5	8

SBRT Lung/Liver/Abdominal Cases

- 4DCT simulation must be done first to access tumor motion range ·
- Gating will be considered only if motion > 0.5cm, and the patient has a regular, reproducible breathing pattern; alternatively, an ITV can be created. ·
- For gating cases, BlueBAGTM without vacuum suction is used as immobilization device. · Abdominal Belt Compression system can be used for some patients ·
- Fiducials necessary for Liver/Abdominal Cases: no other way to visualize tumor.
- CBCT image quality, FOV limitation for lateral tumors.

- If non-gating, may consider one or both arms on the side.
- Non-coplanar beams could be used to compensate for lateral beams.
- If gating is used,
- coplanar beams can be used for some machines, arms on the side could further limits beams. ·
- VMAT is a good option (can not be combined with gating for many machines) ·
- Gating + fixed beam IMRT or EDW is not advisable (takes way too long to deliver), use FIF instead if you must. ·
- Beam arrangement should consider collision possibility for lateral tumors. Keep beams /arcs on the ipsilateral side.

- If no fiducial
- create fluoro beam aperture that hugs GTV.
- If there is fiducials,
- Create fluoro beam aperture that use fiducials as corners. ·
- CBCT alignment with GTV, bony landmark secondary but should be less than 1cm discrepancy.
- Otherwise, reposition patient. ·
- CBCT sometimes do not align well with average sim CT due to breathing variation ·
- Fluoro to verify positioning after CBCT. ·
- Fluoro between fields to monitor setup consistency.

Bottom line for SBRT

- Without an approved plan in the patient's chart, no treatment verification can be done.
- Physics must be present for treatment verification.
- If IMRT, without IMRT QA documented, no 1st treatment should be done.
- Attending must be present for every treatment fraction.
- Physics should be available for every treatment.

What is a ‘Dry Run’?

- Treatment verification
- Reproduce setup
- Verify isocenter
- Clinically mode up each treatment field
- Check beam clearance (collision) :Check any interlock
- ▪ MLC interlock? Reinitialized but can not clear means corruption of MLC files▪ ⇨undeliverable beam
- Potential MU problem? If
- > 1000 for any single field beyond machine capability for non-SRS beams
- Clearly mark immobilization devices after successful dry run.

Conclusions

- SBRT has emerged as a versatile strategy with a wide range of applications for many different types and stages of cancer.

As with any form of radiation therapy:

- careful attention to matters of patient selection
- Technical quality assurance is essential
- For the effective and safe implementation of SBRT.

Future advances will refine our understanding of the :

- Biological mechanisms
- Optimal integration
- Sequencing of SBRT with other anticancer therapies.

Thank you