Brachytherapy in Hepato-billiary Malignancies

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Hepato-biliary Malignancies

- **Primary**
  - Hepato-cellular carcinoma (HCC)
  - Cholangio-carcinoma

- **Metastatic /Secondaries**
  - Colorectum
  - Breast
  - Stomach/GB
  - Lung

Brachytherapy for Hepato-biliary Cancers

- Intra-luminal Brachytherapy: Bile duct
- Interstitial Brachytherapy: Liver tumors

Brachytherapy for Hepato-biliary Cancers

- Basic concepts, Rationale, Practicalities

Brachytherapy for Liver and Biliary Cancers

- Not a frequently discussed topic in conferences
- It is not very popular
- Does not mean, it is clinically ineffective
- **It has high therapeutic potential**

Reasons for Infrequency

- Lack of awareness and knowledge
- Lack of confidence : skilled procedure
- Invasiveness of the procedure
- Availability of contemporary treatments (SBRT)
- Lack randomised studies
- Lack of interest/mindset

Liver Malignancies: General Management

- Surgical resection (~20%)
- Non surgical treatment (~80%)
  - Underlying cirrhosis
  - Multiple lesions
  - Extra-hepatic mets
  - Medically inoperable
  - Lack of expertise

Non-surgical options

- Ablative therapies: RFA, Cryo-ablation, LITT
- Ethanol injection
- TACE
- Chemotherapy
- **Radiation Therapy**
  - **-EBRT (SBRT)**
  - **-Brachytherapy**

Why Brachytherapy ?

Why not SBRT ?

	SBRT	Brachytherapy
Precision	Highly Conformal	Ultra-conformal
Planning time	Time consuming	Short
Duration	3-5 days	1 hour -5 days
Invasive	Non-invasive (financially invasive)	Minimally invasive
Experience	New	Sufficient
cost	Very Costly	Cost effective
Skill	skilled	skilled
Interest	Hype, enthusiasm	Passion

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BRACHYTHERAPY

Brachytherapy 14 (2015) 537e 542

Dosimetric comparison of brachyablation and stereotactic ablative body radiotherapy in the treatment of liver metastasis

J. Daniel Pennington[1], Sang June Park[1], Narine Abgaryan[1], Robyn Banerjee[1], Percy P. Lee[1], Christopher Loh[2], Edward Lee[2], D. Jeffrey Demanes[1], Mitchell Kamrava[1,*]

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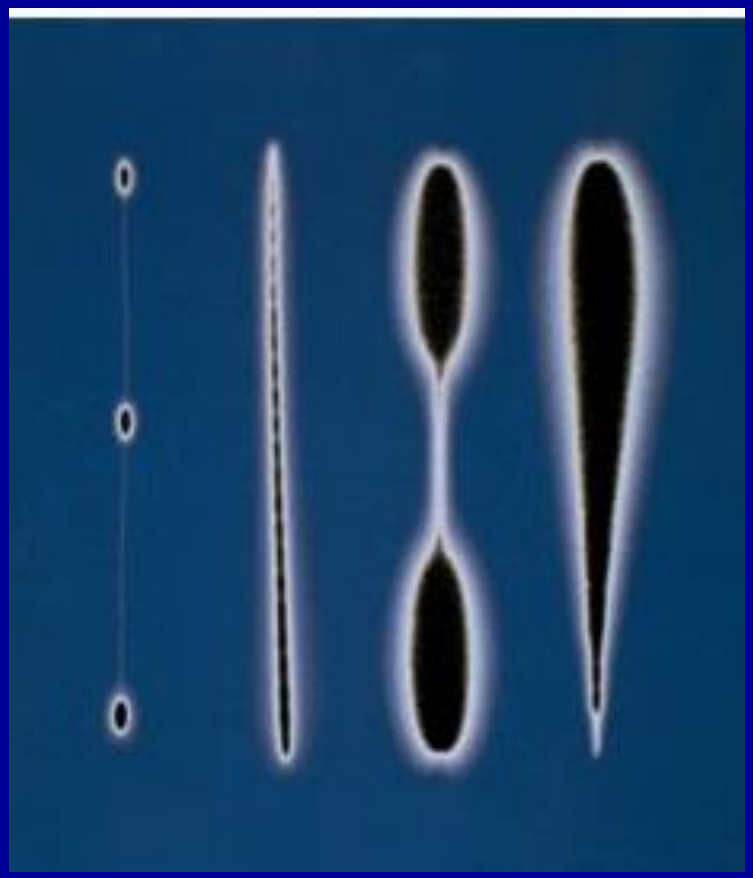
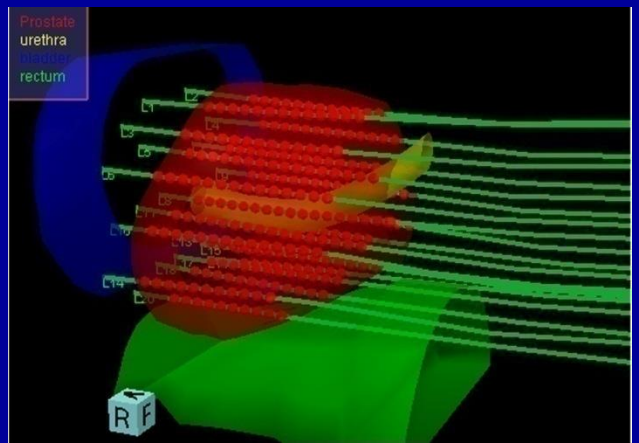
Brachytherapy is like IMRT

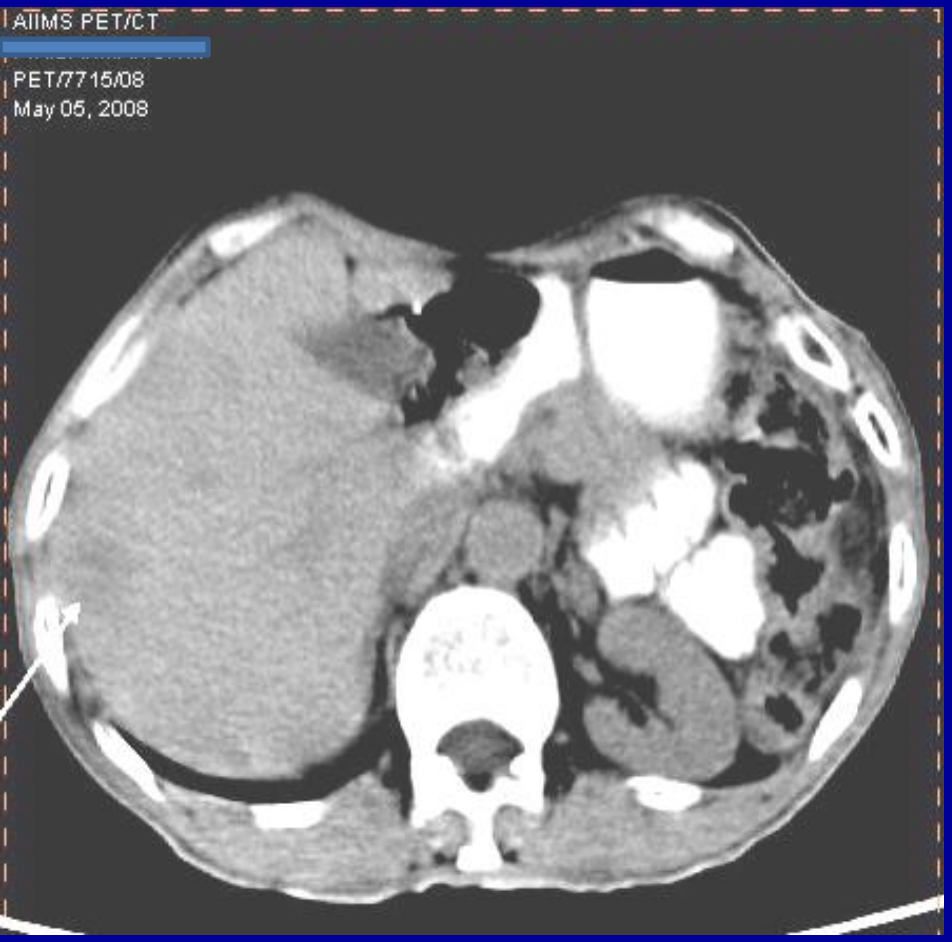
HDR Dose Control

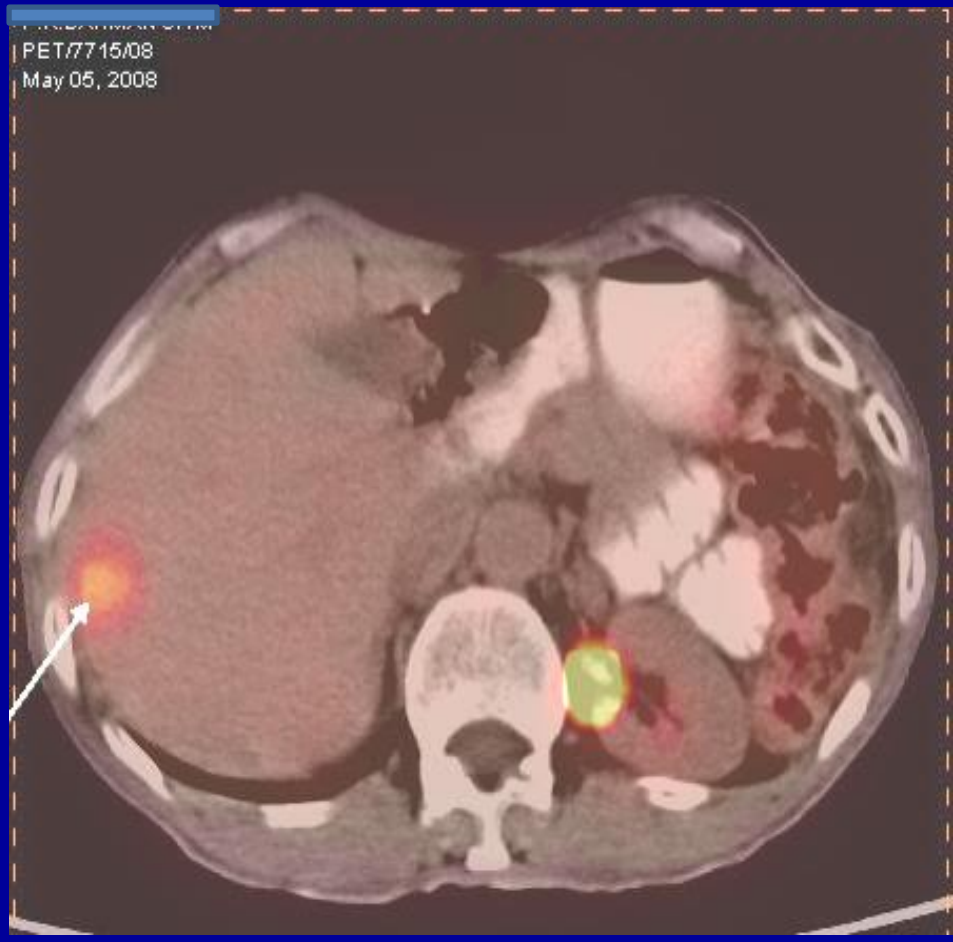
Intensity Modulated Stepping Source

Source strength proportional to dwell time









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Brachytherapy for Liver Lesions

- High-dose-rate Interstitial Brachytherapy
- Seed Brachytherapy
- Selective Internal Brachytherapy (Y-90)

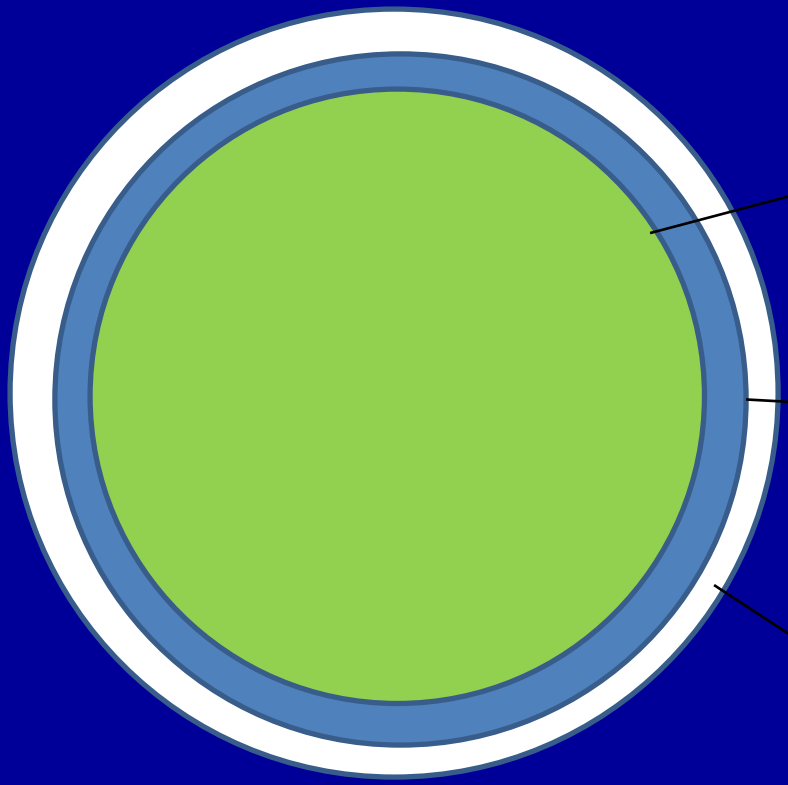
Rationale for using Liver Brachytherapy

- Proven anti-cancer modality
- Successful results in many sites
- Ideal technique for liver lesions (mobility)
- Limited tolerance to RT
- Easy to image: USG, CT Scan, MRI, PET
- Good understanding of Liver tolerance

Liver Tolerance

- Whole liver
  - TD 5/5 : 30 Gy/15#
  - TD 50/5 : 42Gy/21#
- 2/3 of liver
  - TD 5/5 : 50.4Gy/28#
- 1/3 of liver
  - TD 5/5 :68.4GY/38#

Dosimetric advantage of Interstitial Brachytherapy



D3.2cm tumor shell >30Gy

D3.6cm tumor shell>25Gy

D4cm tumor shell>20Gy

RFA VERSUS BRACHYTHERAPY

- Limitations of RFA
  - affected by cooling effect of adjacent large vessels
  - technical difficulty in large tumor (>5cm)
  - not feasible in tumor in proximity to bile duct

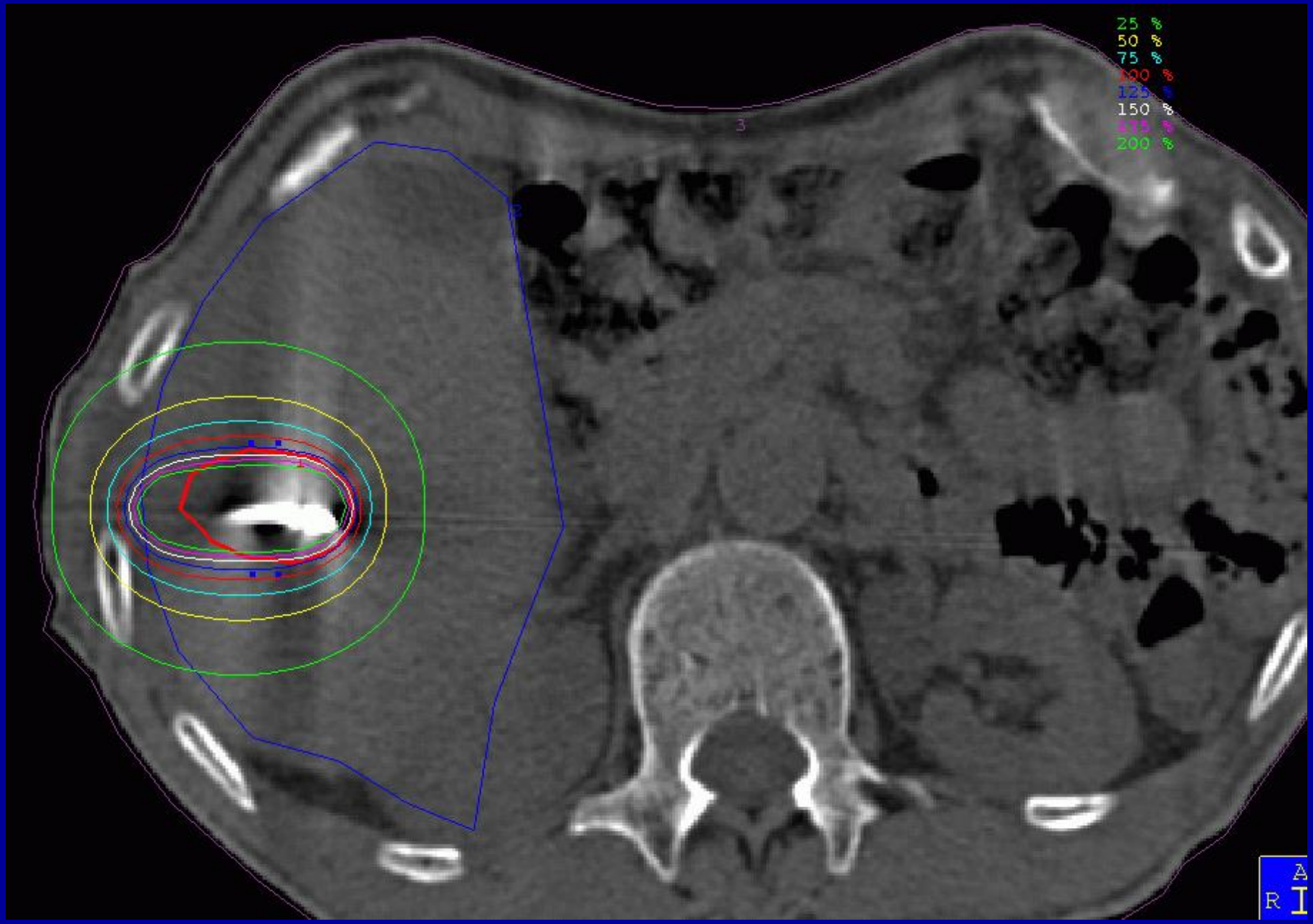
- Advantages of brachytherapy
  - not affected by cooling effect of adjacent large vessels
  - feasible in large tumors (>5cm)
  - feasible in tumors in proximity to bile duct

Indications of IBT liver

- HCC or liver mets
- Any size : preferred for larger lesions
- Even for lesions closer to vessels/ bile duct
- No heat sink effect
- Failures after RFA/SBRT
- Can be combined with thermal ablative procedures

Procedure

- Performed under local anesthesia in CT Room
- Image guidance: USG, CT-scan (preferred)
- 16-G, blind end, steel or rigid plastic needles
- Percutaneous insertion during breath hold
- Single needle for 3 cm and multiple for >3 cm
- Distance between adjacent needles : 2-3 cm
- CT based dosimetry


25 %
50 %
75 %
100 %
125 %
150 %
175 %
200 %
3
2
1
A
R I

Dose prescription & Treatment

- Single HDR dose of ~ 20 Gy by HDR
- Fractionated schedules (6Gy X 5 or 7GyX4)
- Prescribed at the periphery of the PTV
- Dose constraint

  > 33% of liver parenchyma receiving <5 Gy
- Dose to OAR : negligible
- Needles to be removed immediately after Rx
- Overnight stay in ward for observation

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–8, 2009

0360-3016/09/$–see front matter

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doi:10.1016/j.ijrobp.2009.07.1700

CLINICAL INVESTIGATION

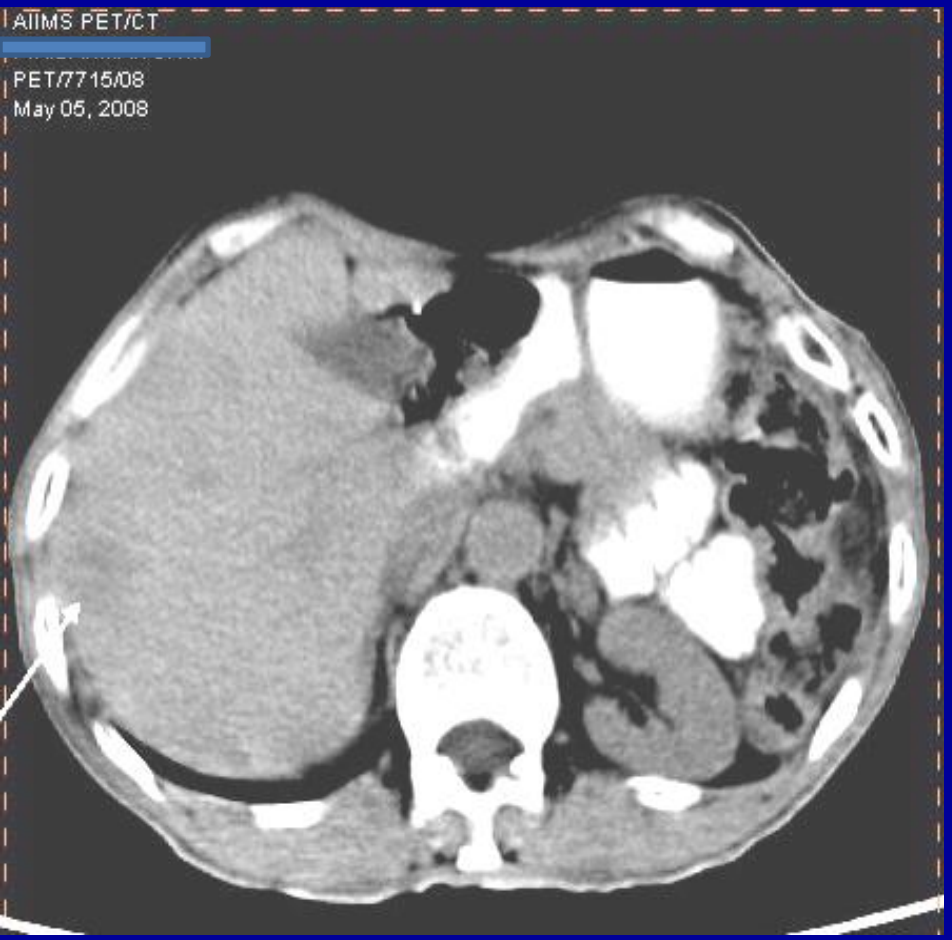
COMPUTED TOMOGRAPHY–GUIDED HIGH-DOSE-RATE BRACHYTHERAPY IN HEPATOCELLULAR CARCINOMA: SAFETY, EFFICACY, AND EFFECT ON SURVIVAL

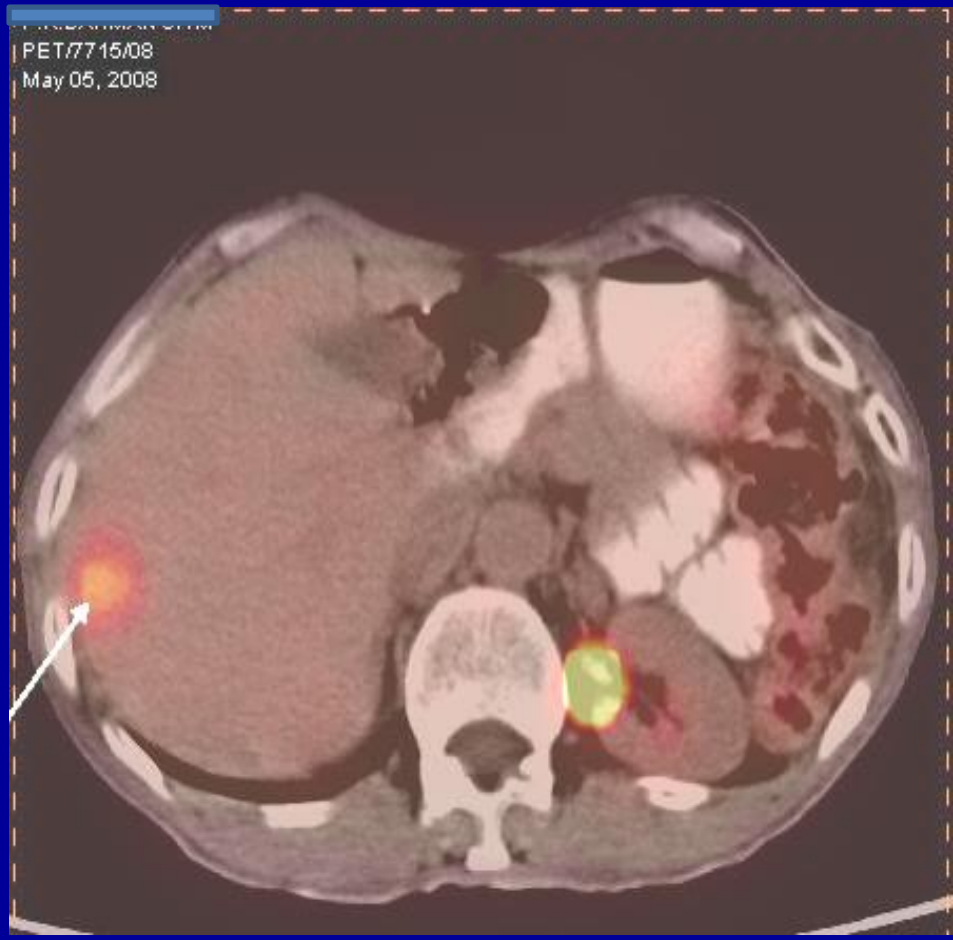
Methods and Materials: A total of 83 patients were recruited, presenting with 140 HCC- lesions. Treatment was performed by CT-guided high-dose-rate (HDR) brachytherapy with an iridium—192 source. The primary endpoint was time to progression; secondary endpoints included local tumor control and overall survival (OS). A matched-pair analysis with patients not receiving brachytherapy was performed. Match criteria included the Cancer of the Liver Italian Program (CLIP) score, alpha-fetoprotein, presence, and extent of multifocal disease. For statistical analysis, Kaplan-Meier and Cox regression were performed.

Results: Mean and median cumulative TTP for all patients (n = 75) were 17.7 and 10.4 months. Five local recurrences were observed. The OS after inclusion reached median times of 19.4 months (all patients), 46.3 months (CLIP score, 0), 20.6 months (CLIP score, 1) 12.7 months, (CLIP score, 2), and 8.3 months (CLIP score, ≥3). The 1— and 3—year OS were 94% and 65% (CLIP score, 0), 69% and 12% (CLIP score, 1), and 48% and 19% (CLIP score, 2), respectively. Nine complications requiring intervention were encountered in 124 interventions. Matched-pair analysis revealed a significantly longer OS for patients undergoing CT-guided brachytherapy.

Conclusion: Based on our results the study treatment could be safely performed. The study treatment had a beneficial effect on OS in patients with advanced HCC,with respect to (and depending on) the CLIP score and compared with OS in a historical control group. A high rate of local control was also observed, regardless of applied dose in a range of 15 to 25 Gy. © 2009 Elsevier Inc.

IBT Liver : Patient 1





IBT Liver : Pre-brachytherapy CT and PET-CT

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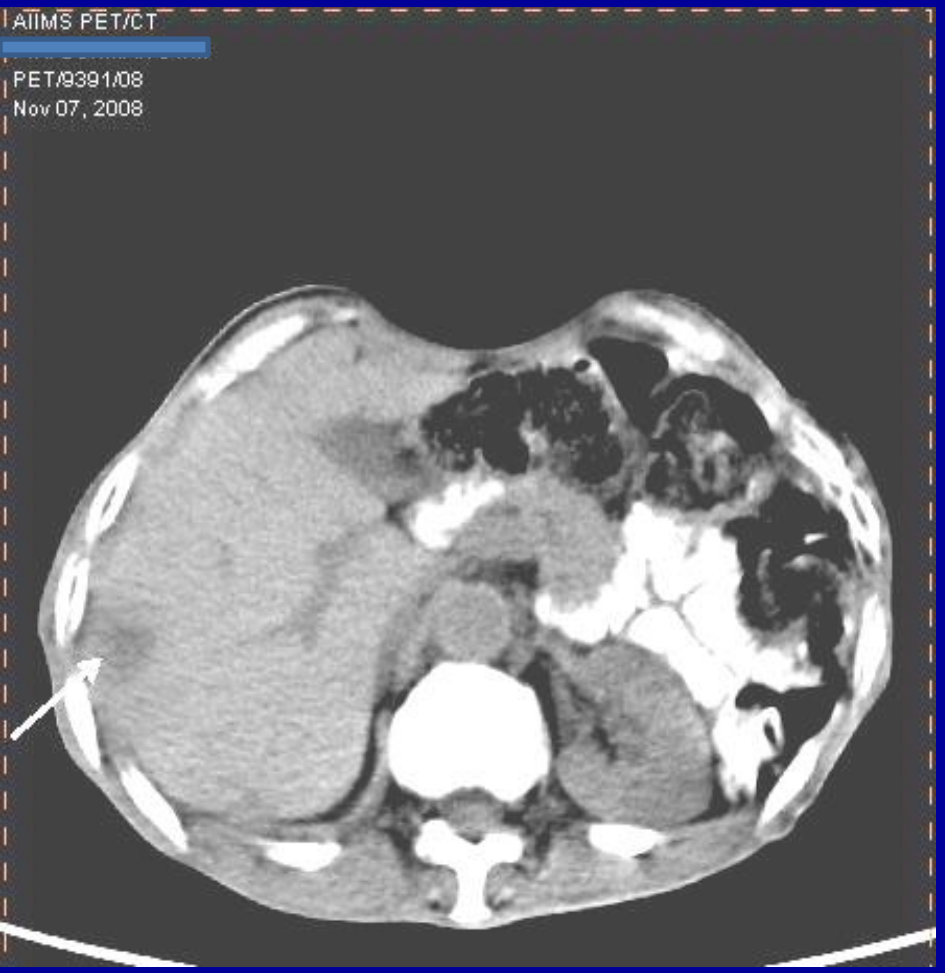
IBT Liver : Patient 1



IBT Liver : Post-brachytherapy CT and PET-CT

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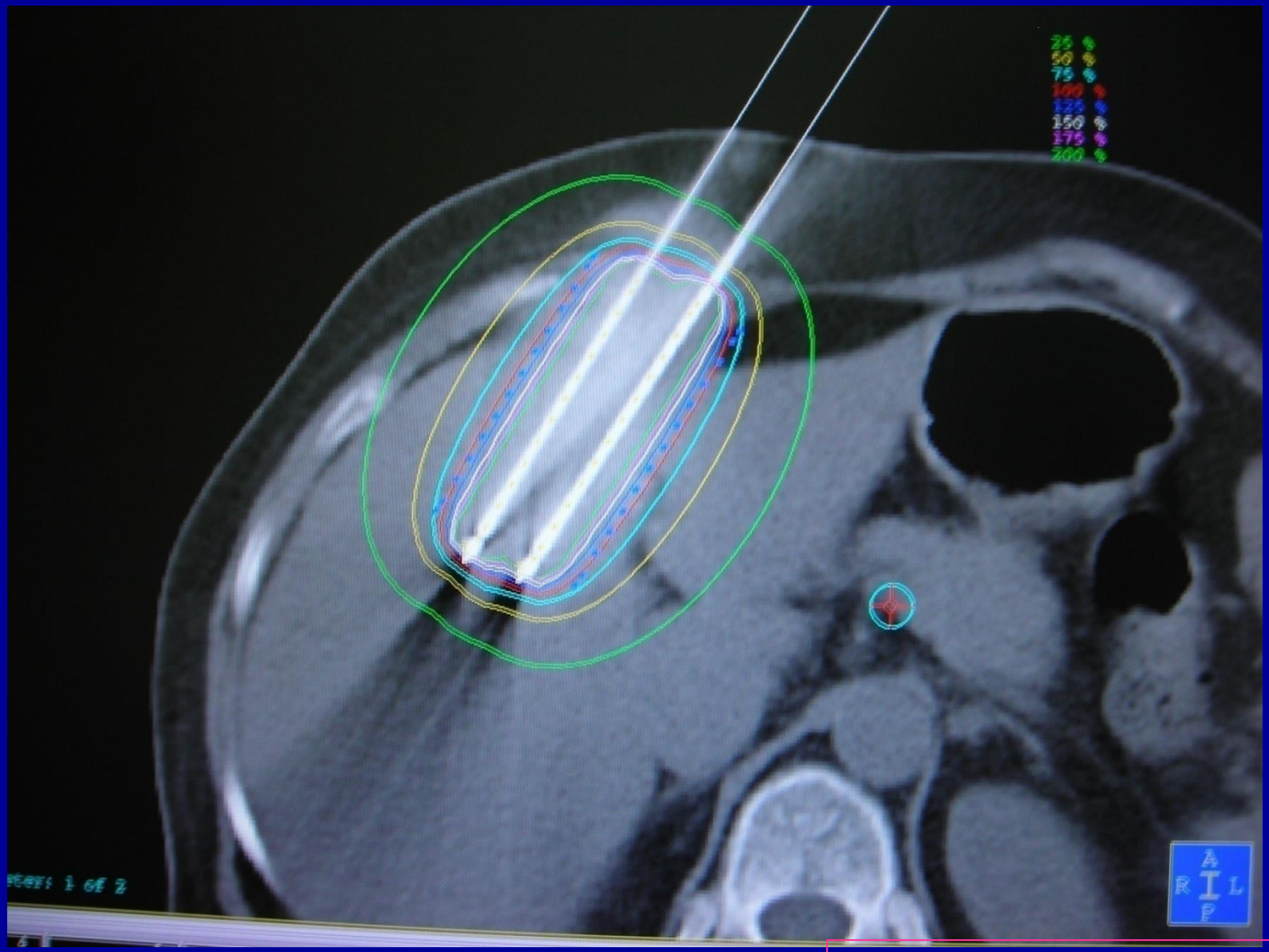
IBT Liver : Patient 2



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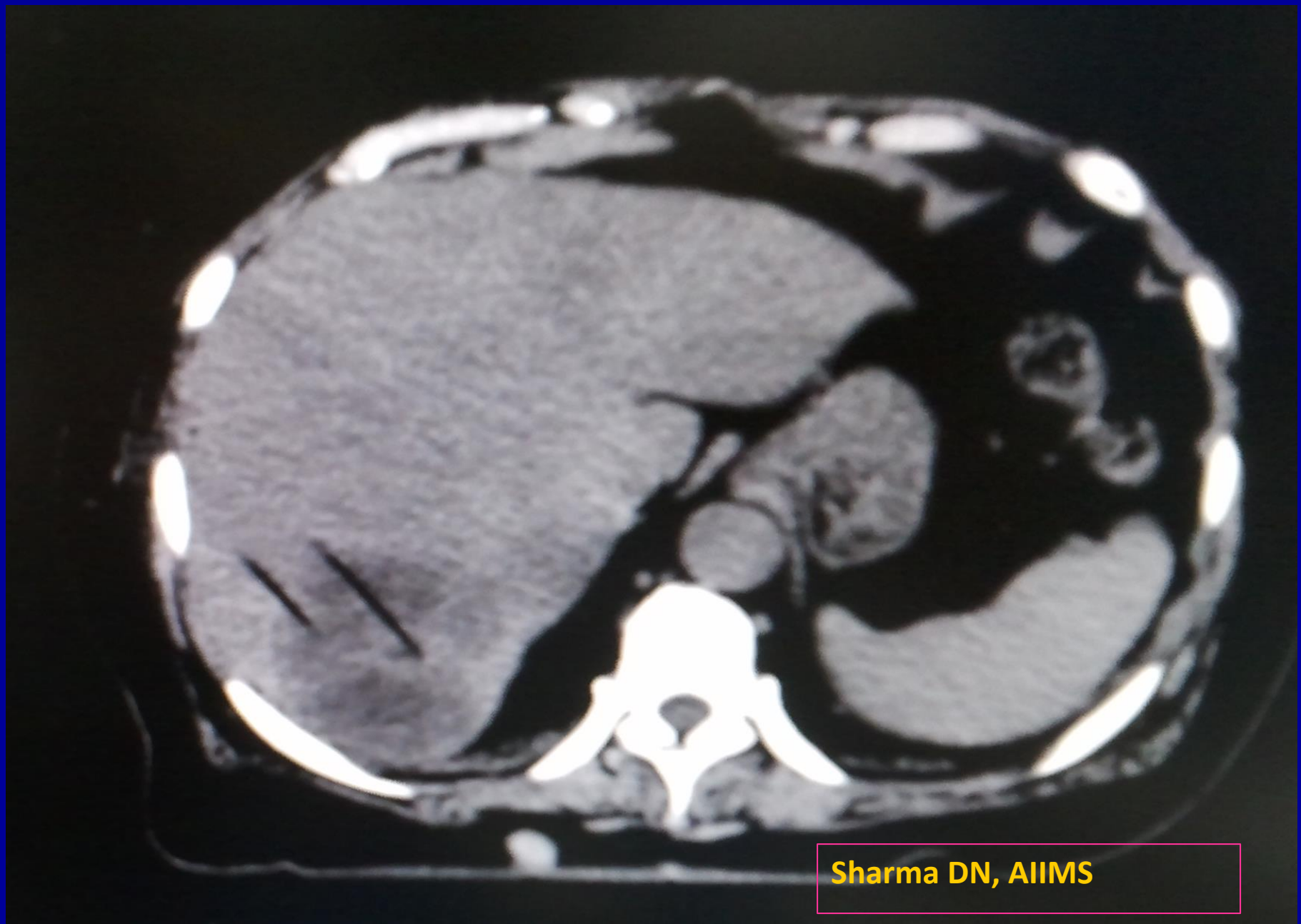
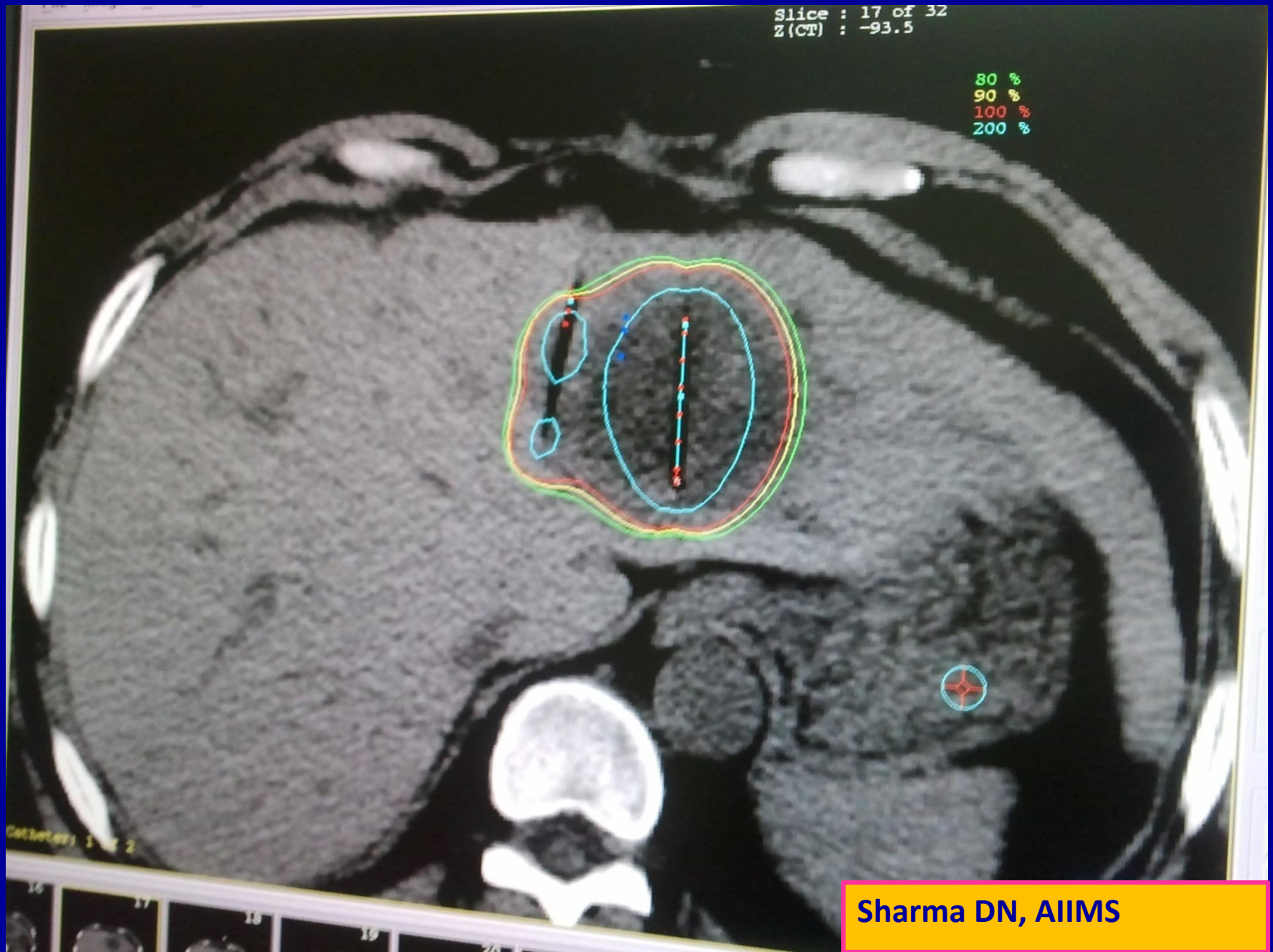
IBT Liver : Patient 3



IBT Liver : Patient 4



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IBT Liver : Patient 5

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CT Guided IBT for Liver Mets: AIIMS Experience

Attribute	
Gender	No. of patients
Male	5
Female	5
Age	Year
Median	54
Range	40-72
Primary site	No. of patients
Breast	3
Colorectal	2
Gall Bladder	2
Stomach	2
Unknown origin	1
Number of lesions	No. of patients
Solitary	8
Two	2
Size of the lesion	cm
Median	3.8
Range	2.7-7.0

CT Guided IBT for Liver Mets: AIIMS Experience

Duration of brachytherapy procedure	**Minutes**
Median	65
Range	50-105
No. of brachytherapy needles	n
Median	2
Range	1-4
Target Volume	**c.c.**
Median	21.3
Range	9-84
V_{100}	**c.c.**
Median	19.6
Range	9.3-83.2

CT Guided IBT for Liver Mets: AIIMS Experience

Complication	No. of patients	Intervention
Abdominal hemorrhage (Major)	0	-
Anaphylaxis/shock due to local anesthetic (Major)	0	-
Pain (Minor)	3	Simple oral analgesics
Nausea/vomiting (Minor)	2	Antiemetic drugs
Asymptomatic pleural effusion (Minor)	1	No active treatment
Abdominal hemorrhage (Major)	0	-
Jaundice (Major)	0	-

Author (Ref.)	Year published	No. of pts	No. of pts with LM	Primary site	Median lesion size (cm)	No. of catheter (median)	Dose (Gy)	Median FU (month)	Local control (%)	Survival	Major complication rate (%)
Ricke et al (7)	2004	20	19	Mixed	5	2-6	17	13	53-71	1-yr PFS, 33%	10
Ricke et al (8)	2004	37	35	Mixed	4.6	NR	17	14	73	1-yr PFS, 34%	5
Ricke et al (9)	2010	73	73	Colo-rectum	3.1	NR	15 20 25	15	75	NR	7.5
Steffen et al (10)	2010	19	19	Colo-rectum	NR	2-6	20	9	60	NR	NR
Wieners et al (11)	2011	41	41	Breast	4.6	NR	18.5	18	93	1-yr PFS, 40%	1.5
Tselis et al (12)	2012	31	23	Mixed	NR	3	13	13	79	1-yr OS, [illegible]	4.7
Sharma et al	-	10	10	Mixed	3.8	2	20	9	75	1-yr PFS, 33%	0

J Contemp Brachytherapy 2013; 5(2): 70-5.

High-dose-rate interstitial brachytherapy for liver metastases: first study from India

Table 2
Clinical summary of trials using brachyablation to treat liver metastasis

Study	Histology	Patients	Dose	Major complications
Ricke, 2004a (2)	Metastatic (36) and cholangiocarcinoma (1)	37	10–20 Gy	1 acute liver failure (concurrent capecitabine) and 1 obstructive jaundice
Ricke, 2004b (3)	Metastatic (19) and cholangiocarcinoma (1)	20	12–25 Gy	1 hemorrhage and 1 obstructive jaundice
Mohnike, 2010 (4)	HCC (140)	83	15–25 Gy (114 lesions), 12–15 Gy × 2, bimonthly (12 patients)	9 complications in 124 interventions: 5 bleeding, 3 abscess, and 1 gastric ulcer
Ricke, 2010 (5)	Colorectal metastases (199)	73	15, 20, or 25 Gy	2 occult bleeding, 2 gastric ulcer, 1 pleural effusion, and 1 anaphylaxis to contrast
Rühl, 2010 (6)	Colorectal metastases (18), breast metastasis (1), and HCC (1)	20	15–25 Gy, retreated 2–4 times	No Grade 2 hematologic toxicity, and no acute or chronic liver dysfunction
Wieners, 2011 (7)	Breast (115)	41	15–25 Gy	1 hemorrhage through puncture site
Collettini, 2012 (8)	HCC (5–12 cm)	35	15–20 Gy	None
Tselis, 2012 (9)	Metastatic (23), HCC or cholangiocarcinoma (8)	31 (42 procedures)	7–32 Gy total in 4–10 Gy BID or 7–14 Gy daily (1–5 fractions)	2 intra-abdominal hemorrhage
Collettini, 2013 (10)	Colorectal (16), breast (9), and other (7)	32	20 Gy	1 biliary abscess
Sharma, 2013 (11)	Metastatic (12)	10	20 Gy	None
Tselis, 2013 (12)	Metastatic (40) and primary liver tumors (10)	41	7–32 Gy total in 4–10 Gy BID or 7–14 Gy daily	2 intra-abdominal hemorrhage and 1 gram-negative sepsis
Brinkhaus, 2014 (13)	HCC (21), colorectal (17), cholangiocarcinoma (9), breast (8), pancreas (6), gastric (3), and other (5)	69	10–20 Gy	Biochemical markers of liver function normalized at 6 wk

Seed Brachytherapy for liver tumors

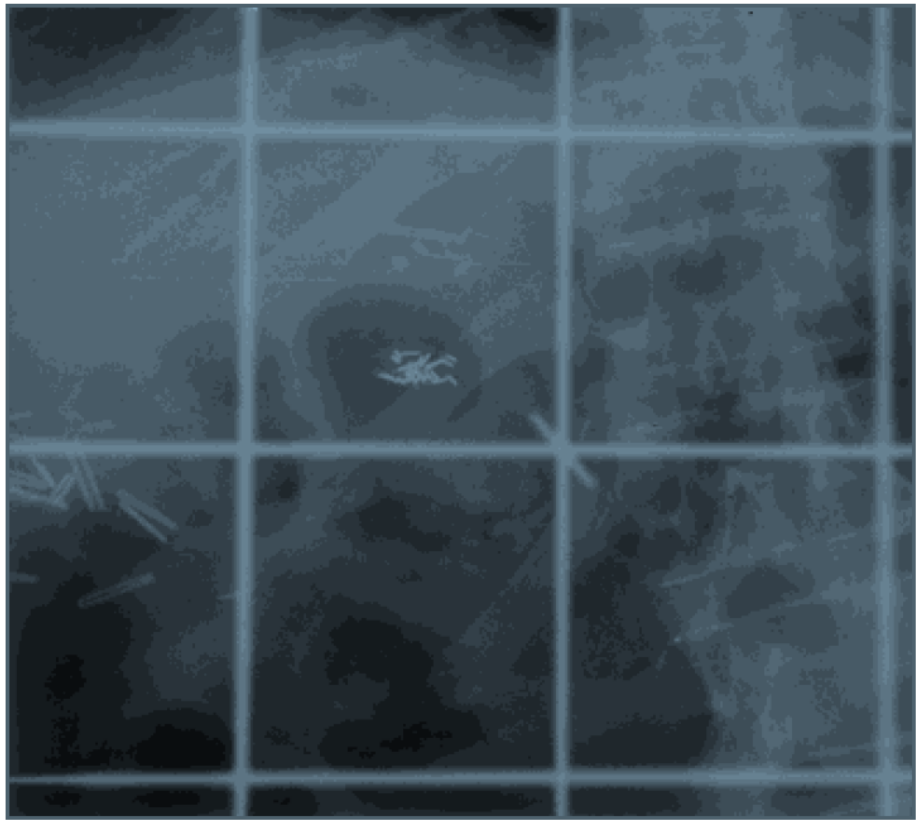
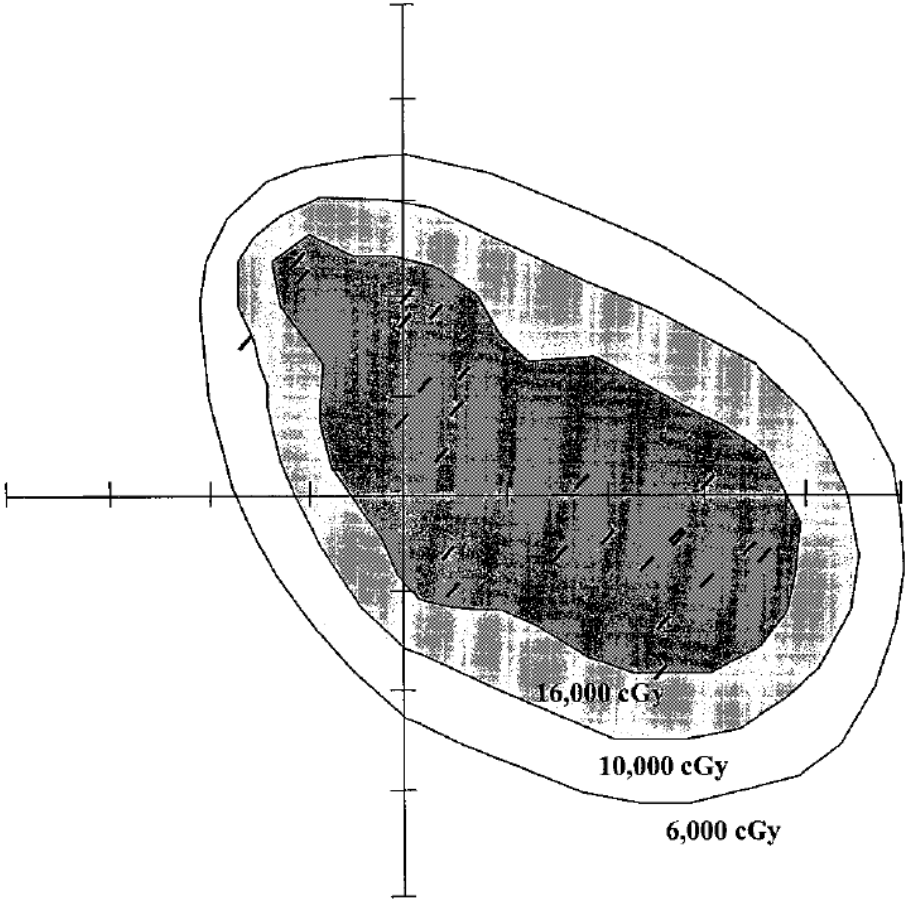


FIGURE 1. Anteroposterior abdominal radiograph showing implanted iodine-125 seeds in a centrally located liver lesion.



International Journal of
Radiation Oncology
biology • physics
Official Journal of the American Society for Radiation Oncology
ASTRO

March 1, 2006 Volume 64, Issue 3, Pages 736–744

Long-term follow-up of patients of intrahepatic malignancies treated with Iodine-125 brachytherapy

Presented at the 47th Annual Meeting of the American Society of Therapeutic Radiology and Oncology (ASTRO), October 16–20, 2005, Denver, CO.

Subir Nag, M.D. (F.A.C.R., F.A.C.R.O.), Megan DeHaan, M.D., Granger Scruggs, M.D., Nina Mayr, M.D., Edward W. Martin, M.D.

Received: July 16, 2005; Received in revised form: August 21, 2005; Accepted: August 22, 2005; Published Online: November 08, 2005

CONCLUSION

- Surgical resection is often the first-line treatment option for hepatic malignancies but only <20% are resectable
- Largely inoperable, hence non surgical options
- Wide spectrum of ablative and focal therapy options
- Image guided brachytherapy is precise, safe and effective
- Suitable for larger lesions unlike RFA, SBRT etc.
- Lesion control rate is about 70%
- Complication rate 5-10%.
- Availability very much limited
- Cost effective

Long Live Brachy.....