Proton therapy 2006: Costs, Facts, Perspectives

Proton therapy in carefully selected cancer patients is one high technology arm of modern radiotherapy

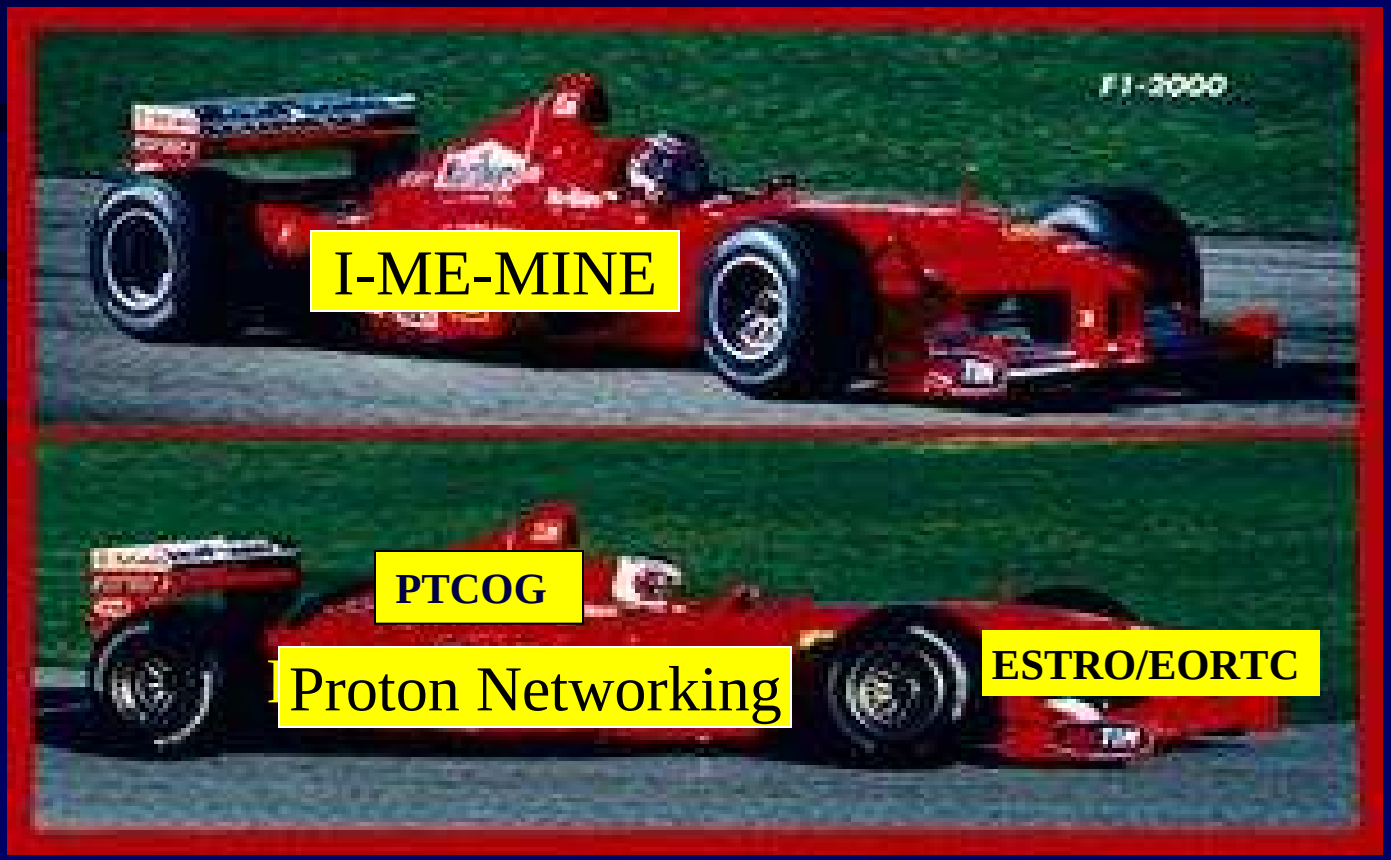
A succesful proton therapy strategy needs more than a brilliant proton accelerator

formula 1 racing ist not just the car:

succesful racing needs powerful sponsors, service crew, research, race tracks, public support ...and a driver

Proton therapy and Formula 1

It is not who‘s fast and first
but who is racing together



Protons: seeding and harvesting

Harvesting is interesting for both farmers and black crows

5 Priorities for Proton therapy in EU

1.) Needs EU agreement of high priority patients

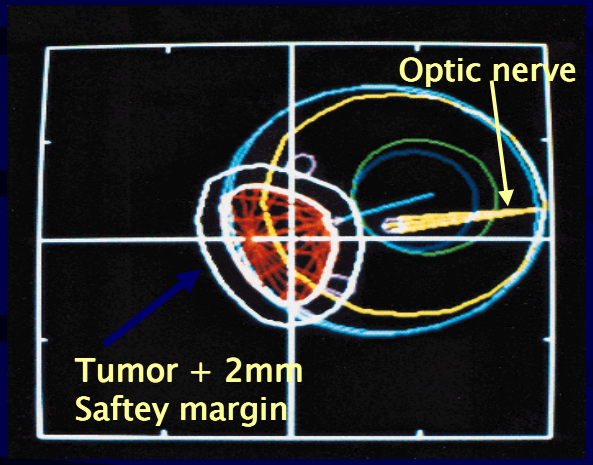
2.) All patients should be treated on protocols incl. 10 y f/u

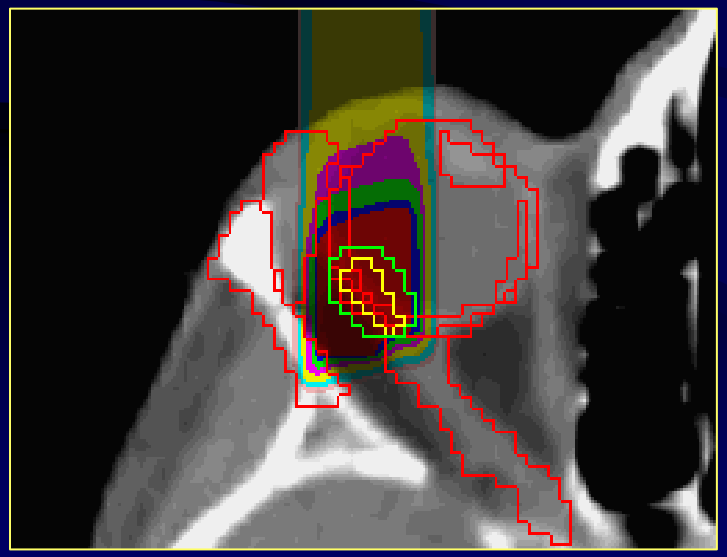
3.) Institutional research focus (unique phase I/II studies)

4.) Electronic patient referral a) comp. planning b) proton RT

5.) Yearly exchange/update of clinical data of all EU proton facilities needed (e.g. ESTRO, EORTC-RT group meetings)

I Uveal melanoma





E.g. PSI experience:

>4500 patients treated

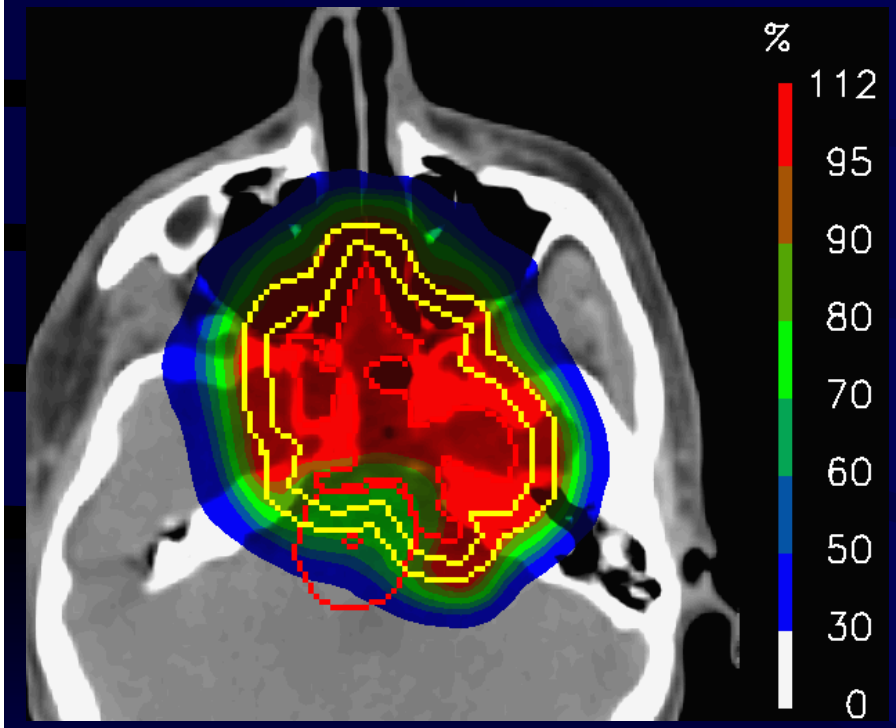
Local control: 98%

Eye retention after 10 years:

100% for small tumours

90% for large tumours

I Skull-base chordoma



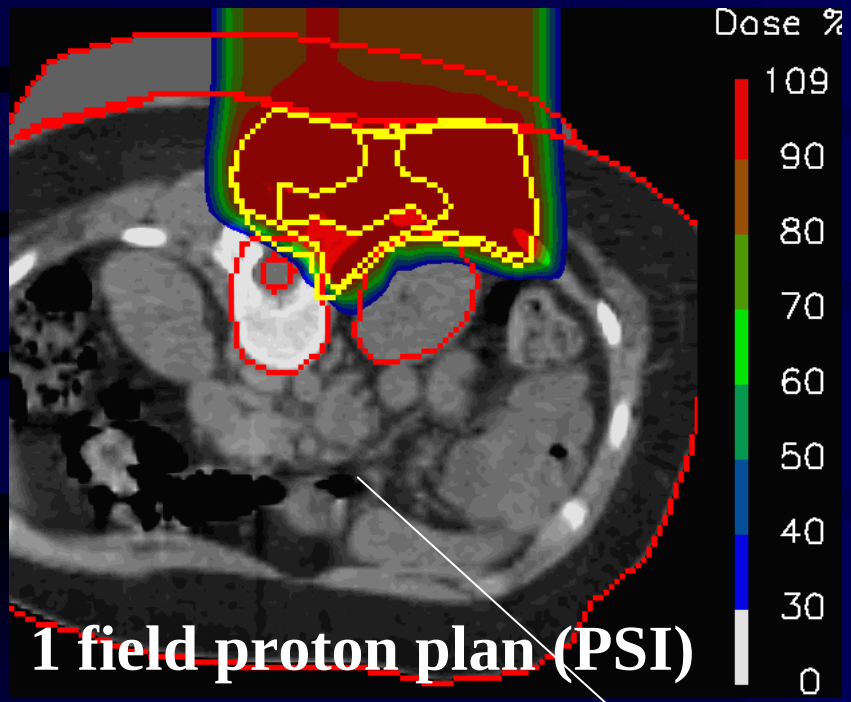
PSI skull-base proton plan

Author	n	Mean dose (CGE)	3-yr LC (%)
Hug[1]	58	71	67
Noel[1]	67	67	71
Schulz-Ertner[3]	67	60	87
Igaki[1]	13	72	67
Weber[2]	18	74	87

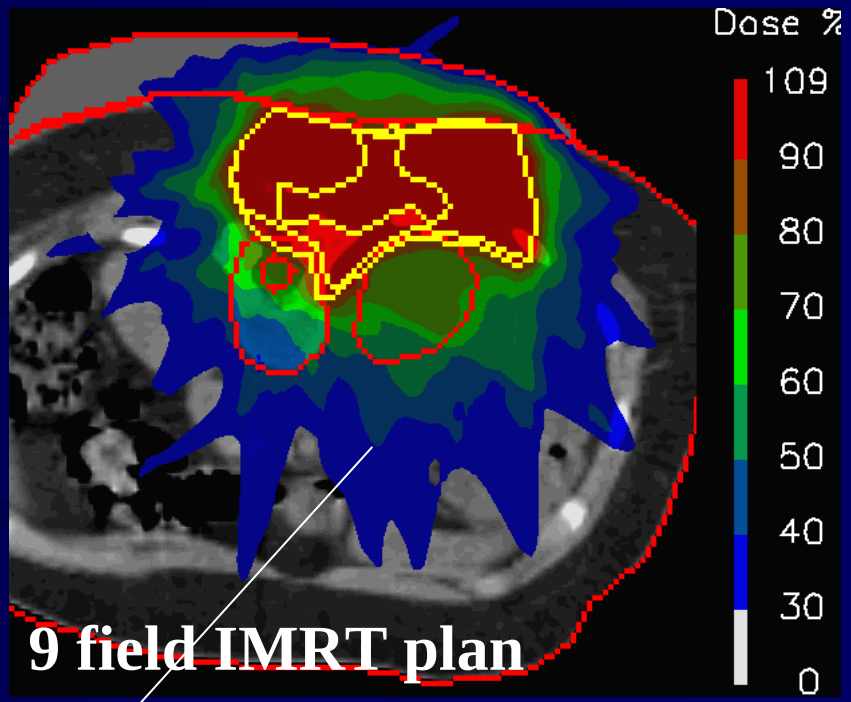
1 X-ray/protons combined
2 Protons only
3 Carbon-ions (3CGE fractions)

II Pediatrics

Desmoid tumor – 12 year old boy



1 field proton plan (PSI)

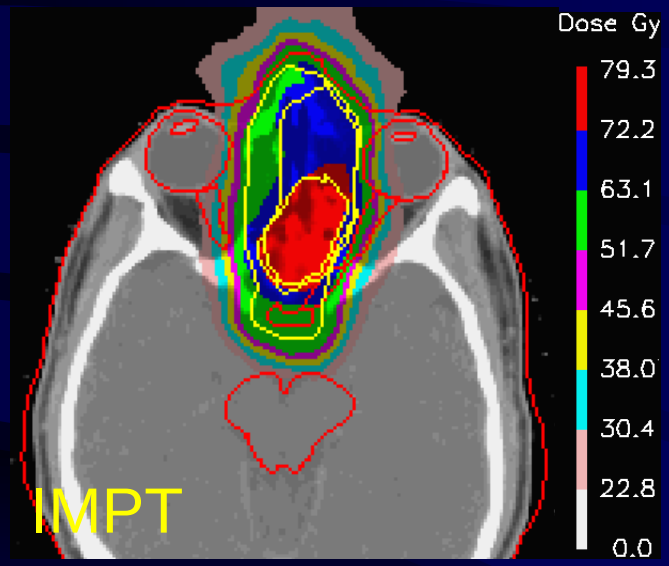


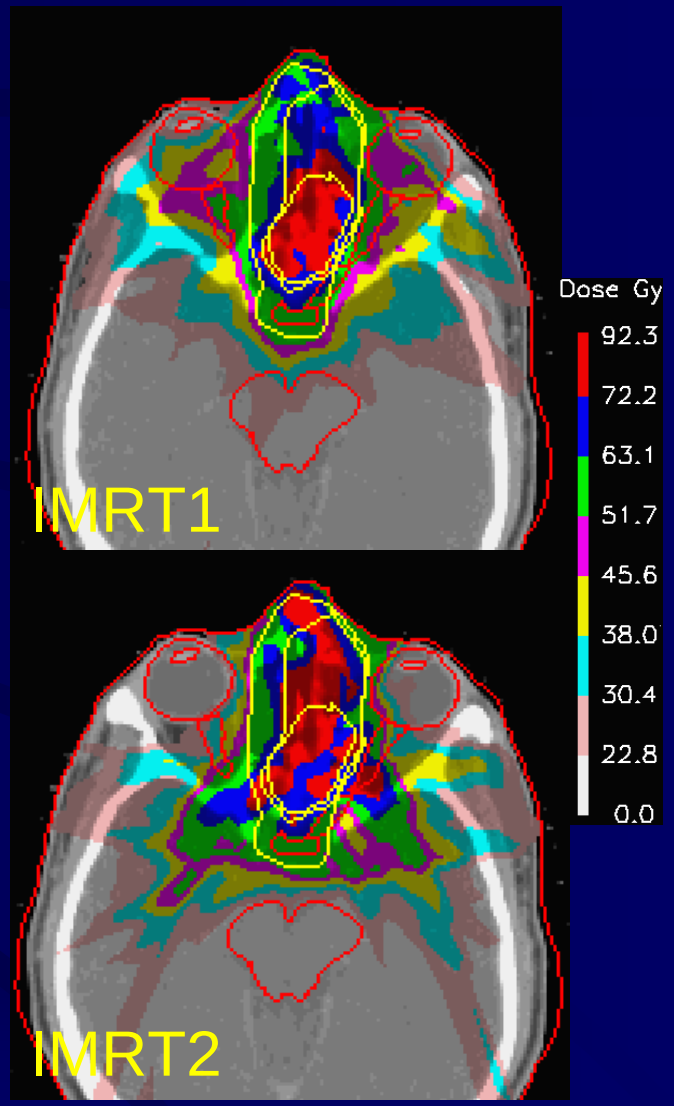
9 field IMRT plan

6 times lower integral dose

(neutrons?)

III Para-nasal sinus cancer





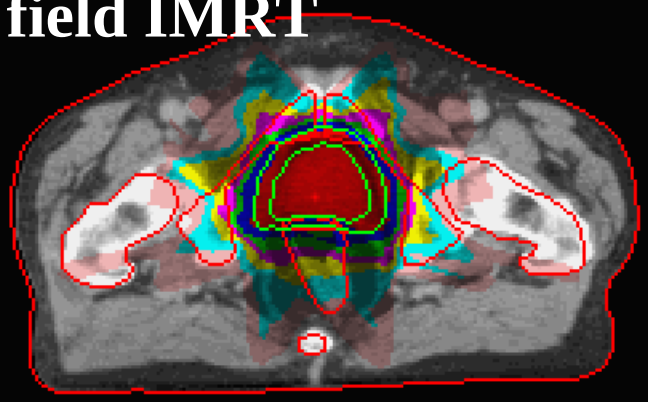
Planning comparison of 9-field IMRT and IMPT

Lomax et al, Radiat. Oncol. 66 (2003) 11-18

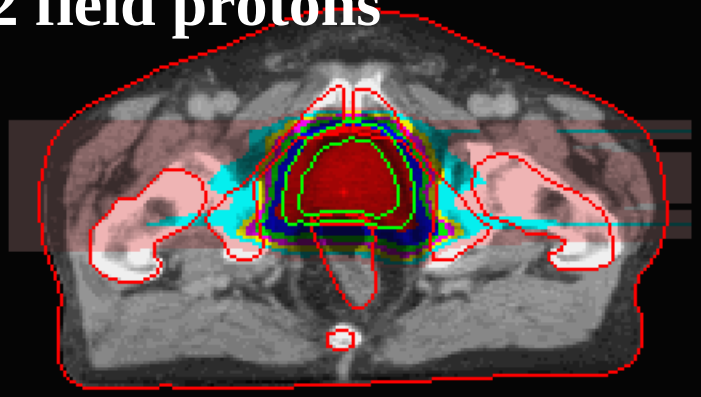
IV Prostate cancer

Planning comparison for prostate

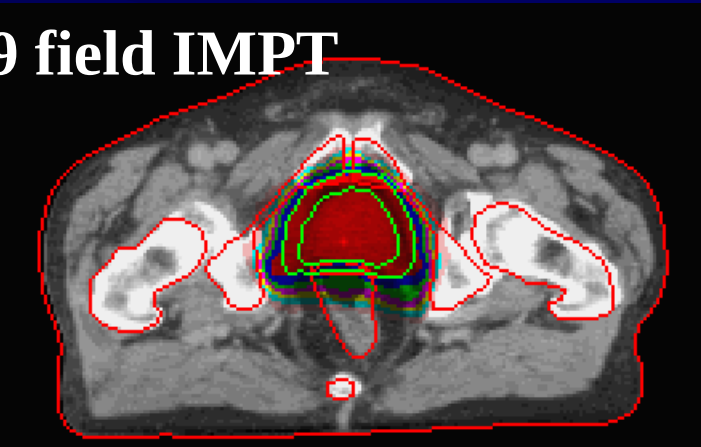
9 field IMRT



2 field protons



9 field IMPT



Little difference in PTV and rectum dose between IMRT, P+ and IMPT

Cella et al, IJROBP, 49 (2001) 217-223

Proposition of 4 categories for proton therapy indications

I current standard of care (evidence based, published data)

II probable indications

geometric advantage with impact on a) LC/DFS b) less grade III/IV long-term toxicities. Must be based on published, peer-reviewed data.

III possible indications

comparative planning studies and / or clinical phase I-II studies required (published comparative planning data, first clinical data)

IV unlikely indications

minimal advantage based on published data

Published Clincal Data for Protontherapy

Clinical data from	Phase III	Phase I-II
Breast Cancer	no	no
CNS tumors (ped./adult)	no	yes
Chordoma-sarcoma	no	yes
Esophagus Cancer	no	no
Head and Neck	no	yes
Lung Cancer	no	yes
Prostate Cancer	(yes)	yes

Prioritisation of protontherapy (1/3)

	Phase I-II	Pre-clinical	Priority
Uveal melanoma	yes	yes	I
Skull base chordoma/ chondrosarcomas	yes	yes	I-II
Pediatric CNS tumors	yes	yes	II
Pediatric sarcomas	yes	yes	II

Prioritisation of protontherapy (2/3)

	Phase I-II	Pre-clinical	Priority
Large, localised, selected solid tumors (adults) (incl. comp. planning)	yes	yes	II
Selected CNS tumors (adults)	yes	yes	II

Prioritisation of protontherapy (3/3)

	Phase I-II	Pre-clinical	Priority
Adv. breast cancer	no	yes	III
Esophagus cancer	yes	yes	III
Adv. head and neck	yes	yes	III
Early stage NSCLC	yes	yes	III
Prostata cancer	yes	yes	III-IV

Protontherapy 2006
selected published results in 5 distinct sites

1.) Skullbase chordomas (Priority I)

2.) Medulloblastomas (Priority II)

3.) Breast cancer (Stage III) (Priority III)

4.) NSCLC (Stage I) (Priority III)

5.) Prostate Cancer (Priority III-IV)

Protontherapy in skull base chordomas / chondrosarcomas

Skullbase chordomas (C)/Chondrosarc.(CS) (**Weber PSI 2005**)

29 consecutive patients, retrospective data, 74 CGe / 68 CGe

median f/u 29 months

RESULTS	**3y act.LCR**	**3y act. OS**	**grade 2 late tox. (CTCAE)**
			(pituitary insufficiency)
chordoma (18)	87.5%	90%	1/18 patients (5.5%)
chondros. (11)	100%	93.8%	3/11 patients (27 %)
photon RT	20-80%		(60-80 Gy, Toxicity ++)

Protontherapy in ped. CNS tumors

Medulloblastoma / Comparative planing

1 comparative plan for 3D, IMRT, Protons (Tarbell, MGH, 2004)

Defined organ at risk receiving 5% and 50% of prescribed dose

RESULTS	3D	IMRT	Protons
pituitary gld.(5/50%)	96/85	31/27	1/0.5
heart (5/50%)	72/84	45/30	2.5/0.5
right lung (5/50%)	94/9.5	75/37	70/0.7
right kidney (5/50%)	86/7	50/36	30/0.6

Protontherapy in ped. CNS tumors

Medulloblastoma / Comparative planing

2nd cancer risk with spinalaxis RT (Miralbell,HCUGE 2002)

RT: 36 Gy/20 fx, whole spine

Estimated absolute yearly rate of 2nd cancer incidence after radiotherapy

RESULTS	**3D**	**IMRT**	**Protons**
Lung	0.07	0.07	0.01
GI-tumors	0.3	0.28	0
all 2nd cancers	0.75	0.43	0.05

Protontherapy in adv. breast cancer

1.) Selection of stage III left sided BC patients

a) improved DFS with locoregional PT (LC, long-term toxicity)

b) OS > 15 years after PT

c) geometric advantage for PT (comparative planing)

2.)<5% patients with left sided Stage III BC qualify for PT

a) improved LC with better PTV coverage

b) decreased cardiac toxicity (coronary artery disease)

Sources: Lundkvist et al, 2002; Van den Bogart 2005

Protontherapy in Stage I NSCLC

Clinical Data **(Nihei, 2006, Chiba)**

37 patients, 1999-2003, all stage I NSCLC, f/u 2 years

Dose 70-94 GYe in 20 x 3.5- 4.9 GYe 5 x /weeks

RESULTS	**2 y OS**	**2y LC**	
stage IA	80%	79%	
stage IB	84%	60%	
grade 2/3 tox	1/17	5/20	(pulm. toxicity)

Benefit for RT-dose escalation if small RT-Volume

Protontherapy in Prostate cancer

Clinical data (Slater, Loma Linda, 2004)

1255 patients, 1991-1997, Stage T1-T3 (T1c 26%, T2c 23%),

51% PSA 4-10, 29% PSA 10-20; 75% Gleason 5-7; med. f/u 62 months

RESULTS

8y Biochemical DFS		73%		
8y Biochem. DFS	PSA 4-10	81%	PSA 10-20	62%
8y Biochem. DFS	Nadir <0.51	87%	<1.0 ng/mL	69%
8y Biochem. DFS	Gleason5-7	73%	Gleason8-10	50%

Protontherapy in Prostate cancer

Dose escalation with photon vs proton boost (Shipley, MGH, 1995)

202 patients, stage cT3/cT4M0, 1982-1992, no hormone therapy

RESULTS	Randomised phase III for dose escalation (boost)	
	photon boost	proton boost
	50.4 plus 16.8 Gy	50.4 plus 25.2 Cg
LC 8y	60%	80% (non significant)
LC 8y Gleason 8-10	19%	84% (significant)

(subgroup analysis in 57 of 202 patients)

Cost comparison (1): Assumptions

- Assume new ‘green field’ proton or X-ray facility
  - Proton facility: Accelerator + 2 gantries
  - X-ray facility: 2 x IMRT LINACS
- Equipment costs:
  - Proton facility 36.8 M€
  - X-ray facility 3.4 M€ (2x1.7M€)
  - Maintenance contract 5.5% of purchase price
- Total construction costs:
  - Include equipment, building, project management, computer infrastructure etc.
- Operational costs:
  - Include personnel, equipment, building and business costs (e.g. repayment of initial investment over 15 years)

Source Goitein and Jermann, Clin.Oncol. 15 (2003) S37-S50

Cost comparison (2): Results

Investments costs

	Protons (M€)	X-rays (M€)
Project management	2.7	0.1
Equipment	38.6	6.8
Building	16.2	5.9
Infrastructure	5.0	4.0
Total	**62.5**	**16.8**

Total operating costs/year (including repayment)

	Protons (M€)	X-rays (M€)
Personnel	4.2	3.3
Equipment	3.2	0.2
Building	0.7	0.4
Business	7.2	2.5
Total	**15.3**	**6.4**

- **Cost ratio (protons/IMRT) ~ 2.4**
- **In 5-10 years ~ 2.1 (reduction of proton equipment costs)**

Source Goitein and Jermann, Clin.Oncol. 15 (2003) S37-S50

Proton therapy: priorities/networks

1.) <u>Patient selection</u>: Electronic patient referral -> 3 step decision

a) consider comparative planning

b) consider proton therapy

c) availability/priority or proton therapy

2.) <u>Prioritisation</u> („comparable“ to bone marrow transplantation)

I-II established indications / pediatric patients (high priority slots)

III adult patients treated on natl./intl. protocols (selected indications)

Source: e.g.Keole et al, Univ. Florida College of Medicine

Thank you all for input and advice

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MGH/Harvard Medical University: Jacob Flanz MD

University Florida Medical College: Sameer Keole MD

Univ. Hospital Essen: Martin Stuschke MD