Medical Physics Aspects of Radiotherapy with Ions

Physics technologies in medicine (4/4)

CERN, Geneva

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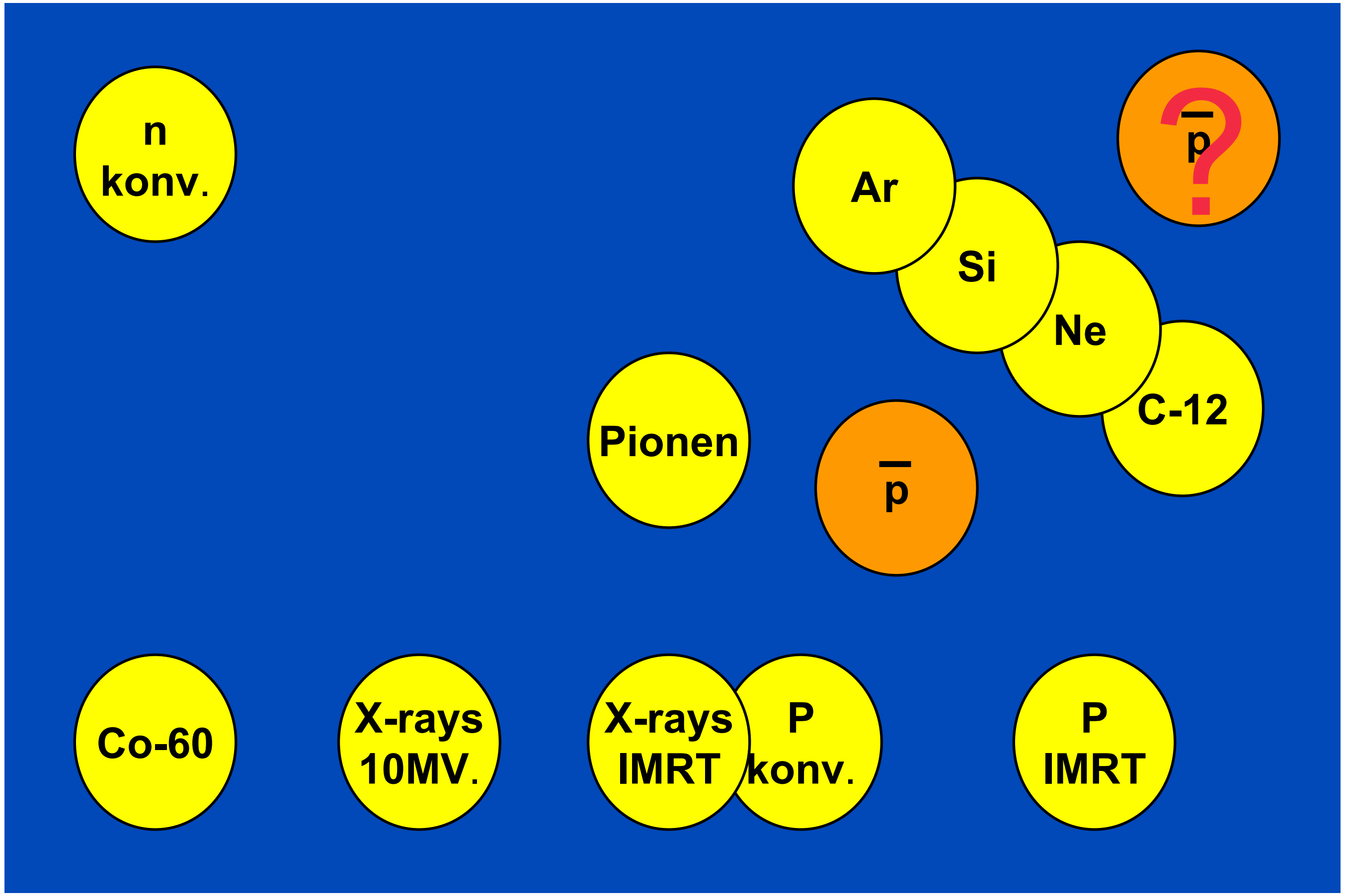
dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

Hadrons in radiation therapy

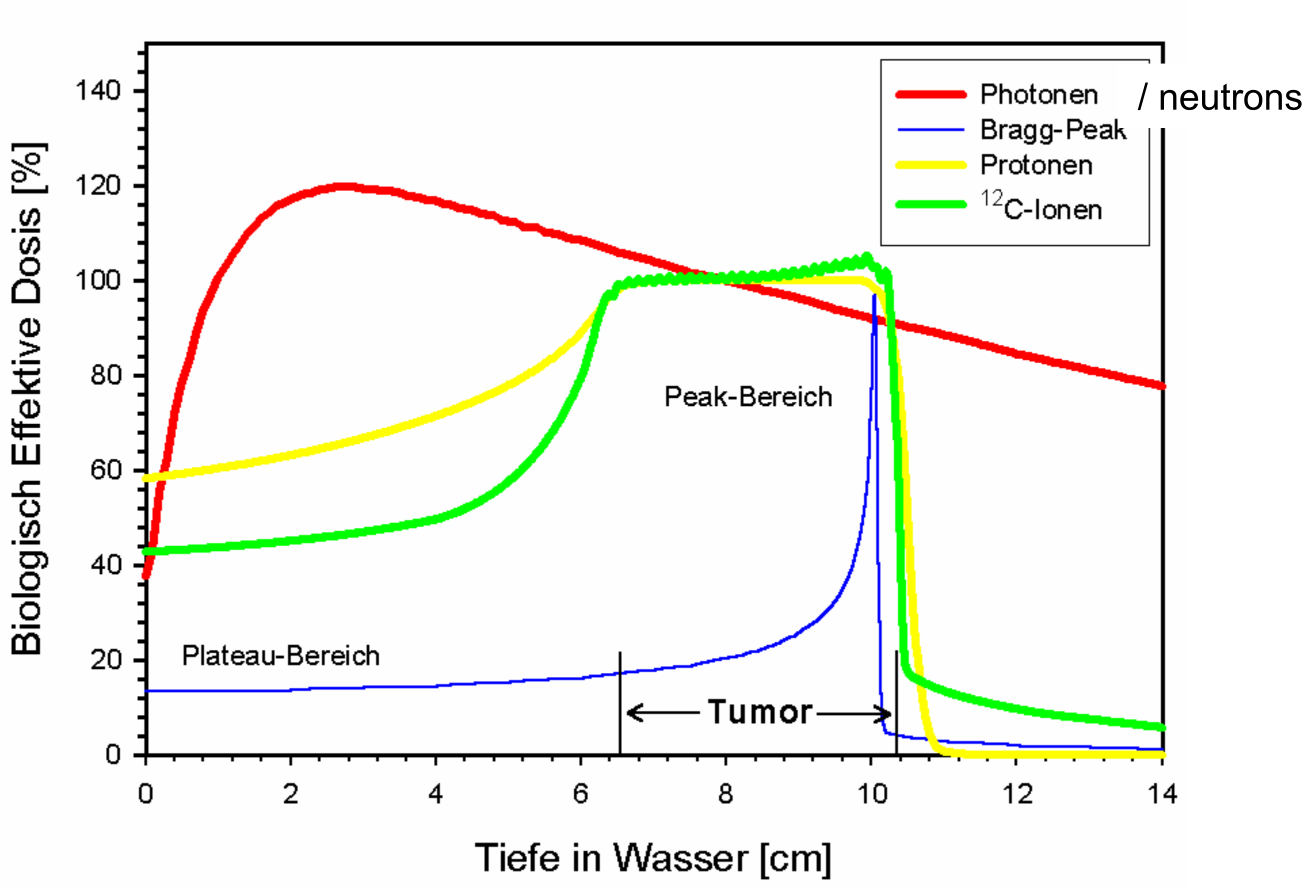
Comparisons of protons, neutrons, pions, ions, photons



Biologival effectivity

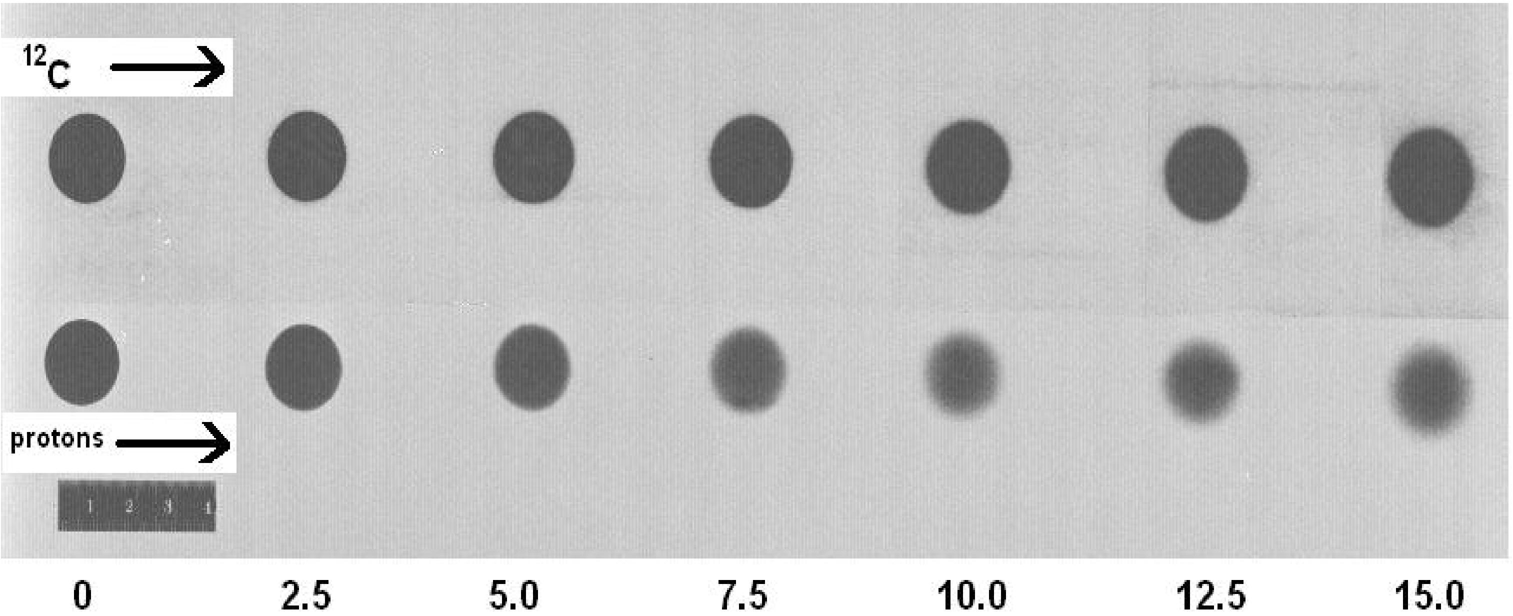
Dose conformation

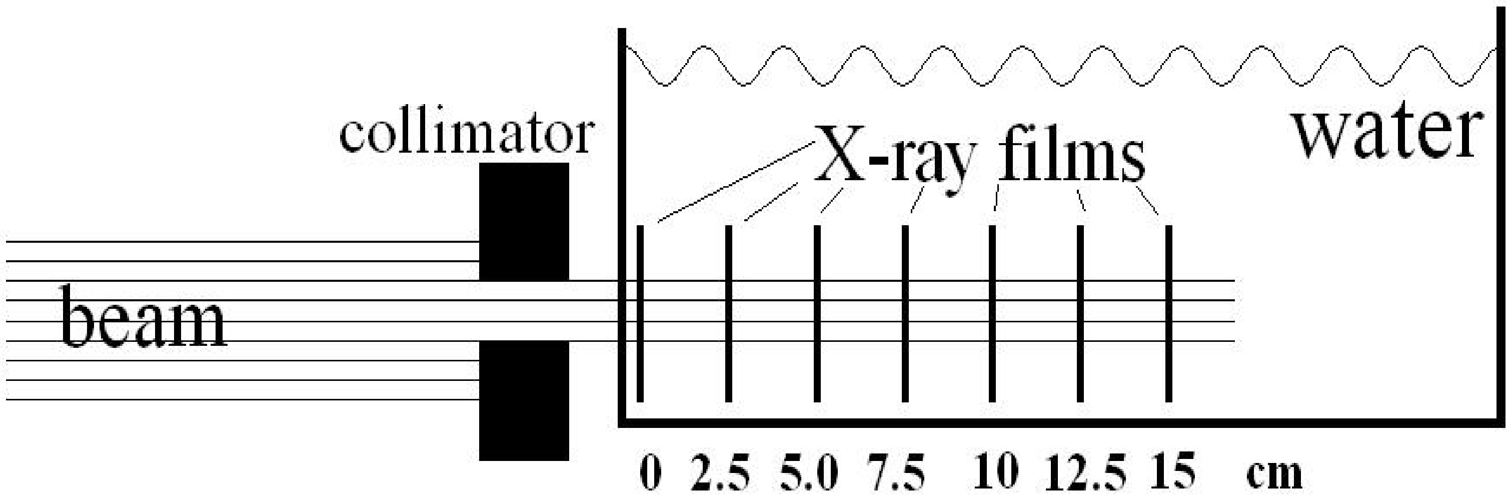
Depth dose distributions of hadron beams



- Neutrons are very similar to photons in terms of depth dose
- Ions show reduced entrance dose and no/little dose behind the Bragg peak

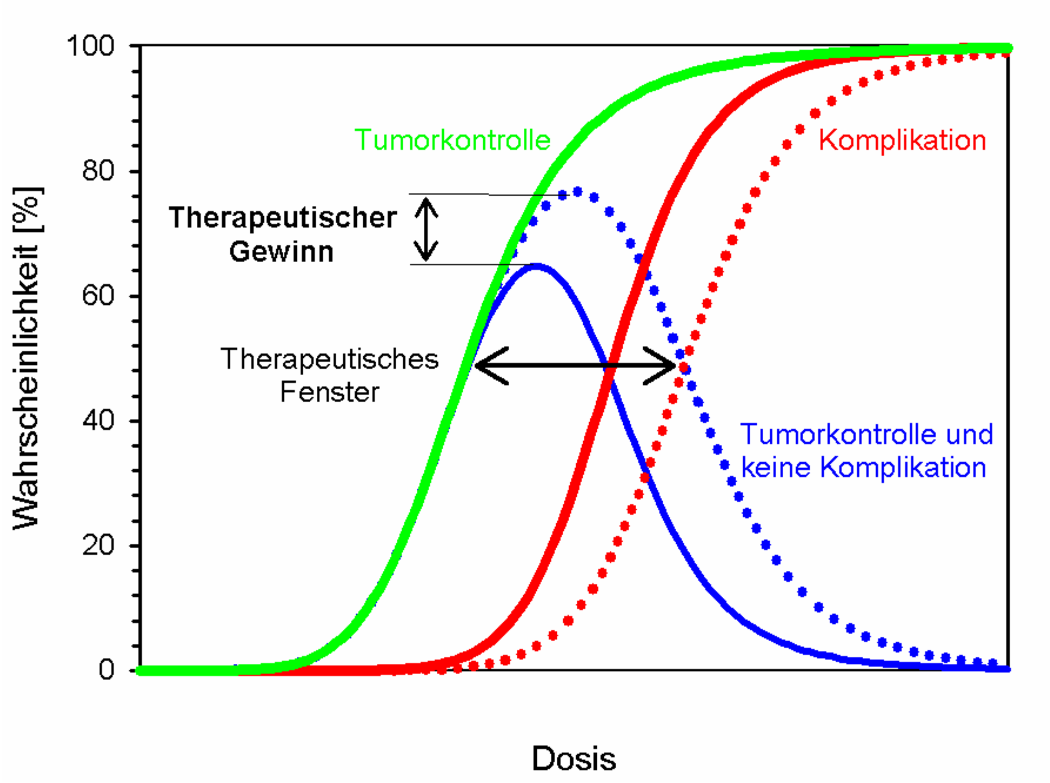
Lateral scattering of carbon ions vs. protons





The Rationale for Conformal Radiation Therapy

- Dose limitation (and TCP-Limitation) due to tolerance of OAR
- Volume effect: increase of tolerance if smaller volume irradiated

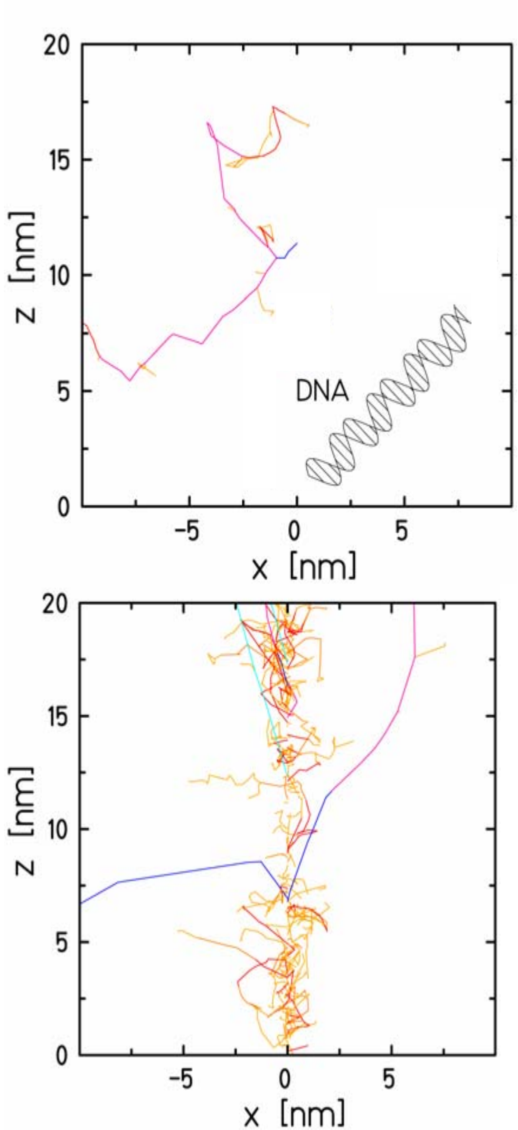


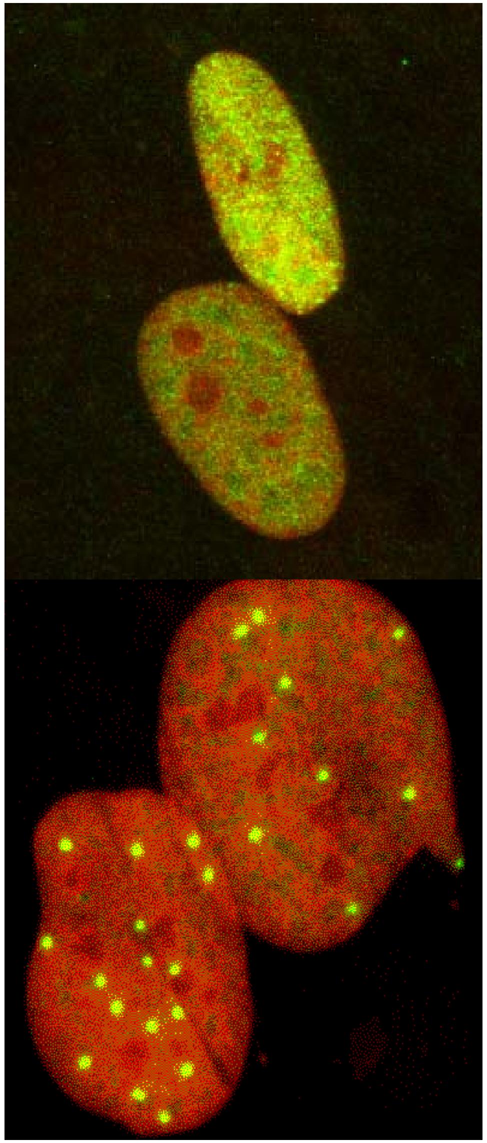
Better conformation of dose enables application of higher doses & higher tumor control without increasing normal tissue complication rate

Radiobiology of high and low LET radiation

Ionization tracks

Damage in nucleus





Low LET

Homogeneous deposition of dose

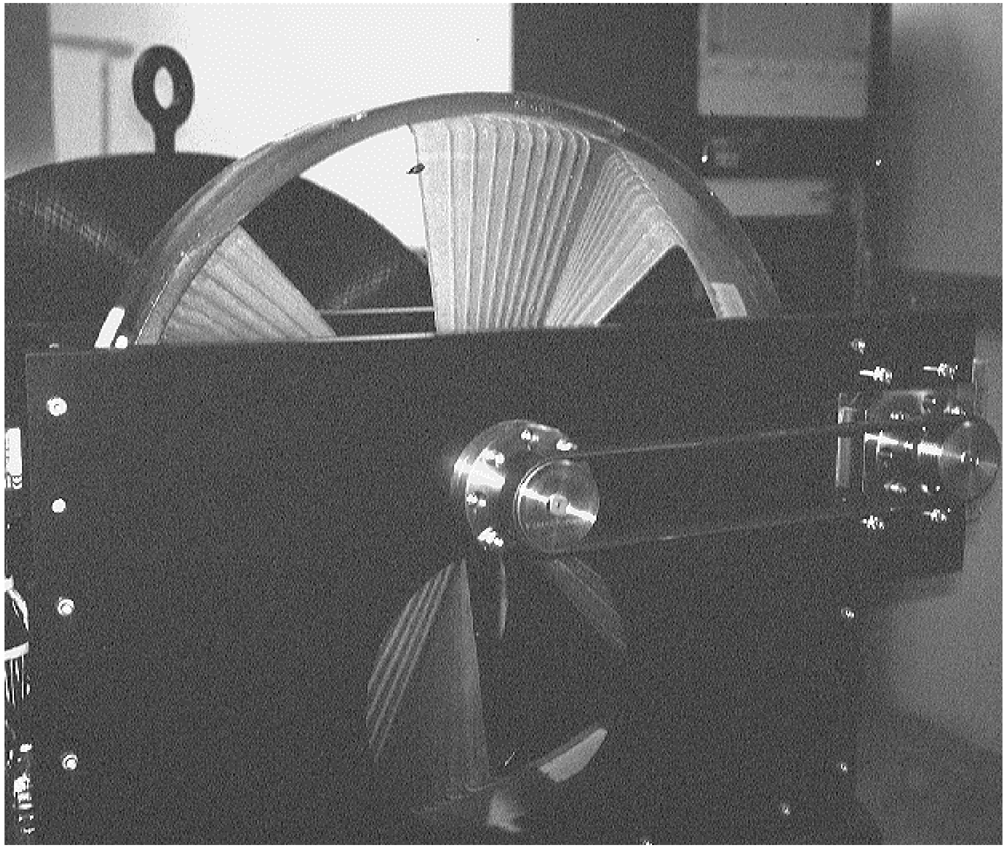
High LET

Local deposition of high doses

M. Scholz et al. Rad. Res. 2001
Immunoflourescence image of the repair protein p21;

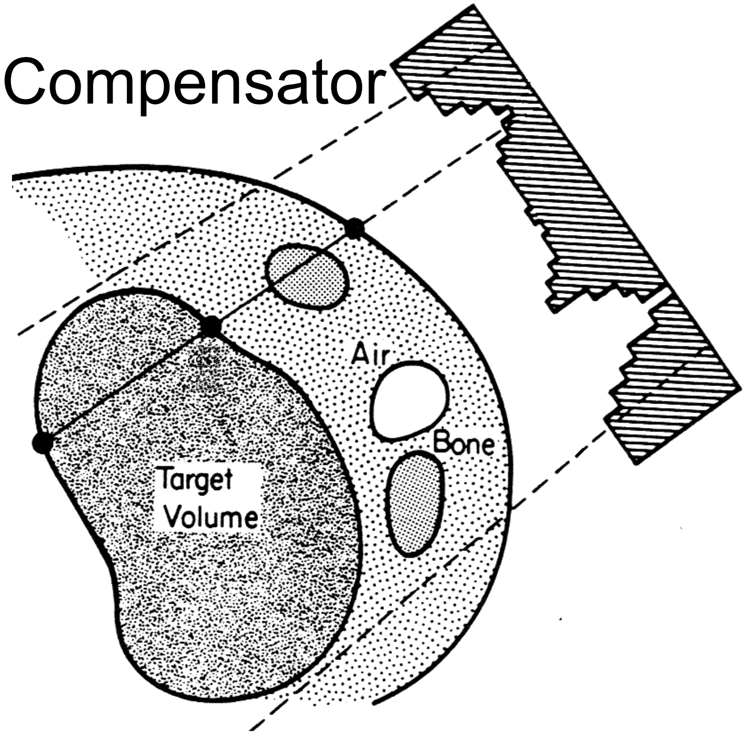
Passive beam shaping
(standard method)

Range modulator wheel



Collimator

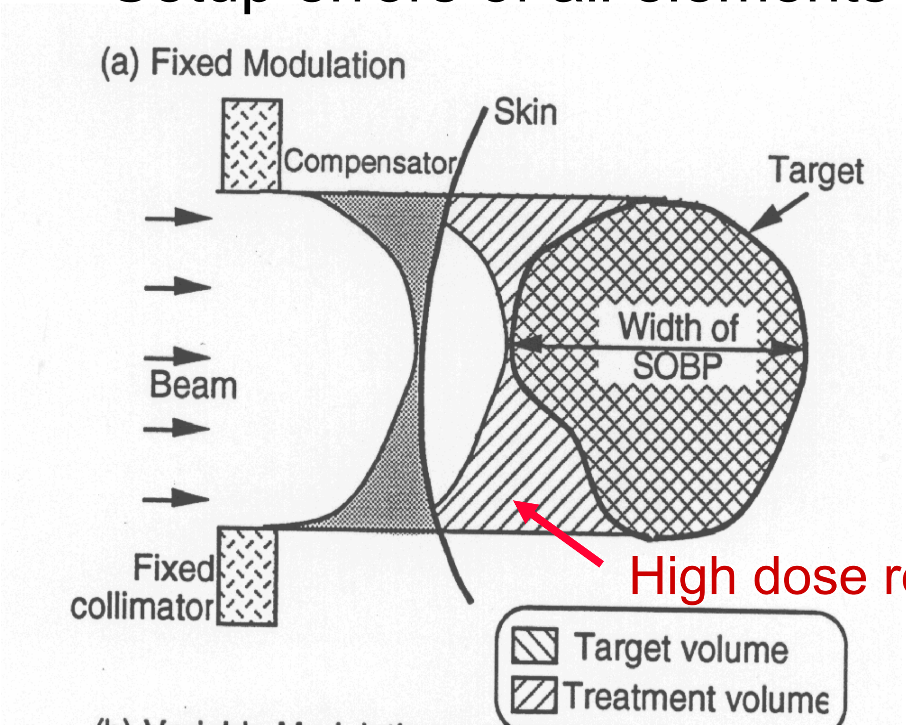
Compensator



TPS for passive beam shaping

Patient specific hardware needed:

- Optimization of Spread Out Bragg Peak, compensator and collimator
- Setup errors of all elements must be considered



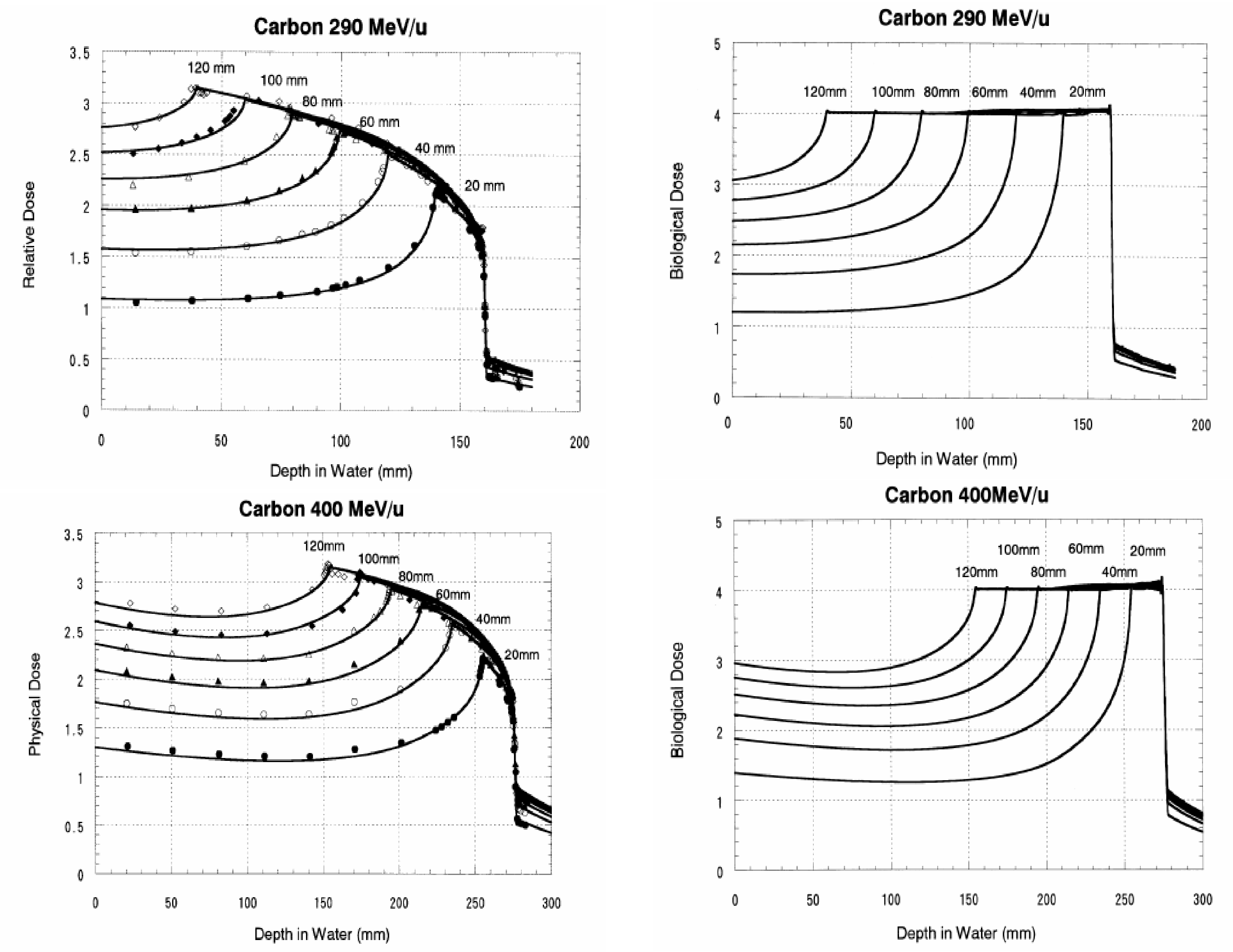
High dose region

SOBP has a fixed extension

Dose conformation only at distal end

- Only measured depth doses needed
- No detailled biological modelling needed

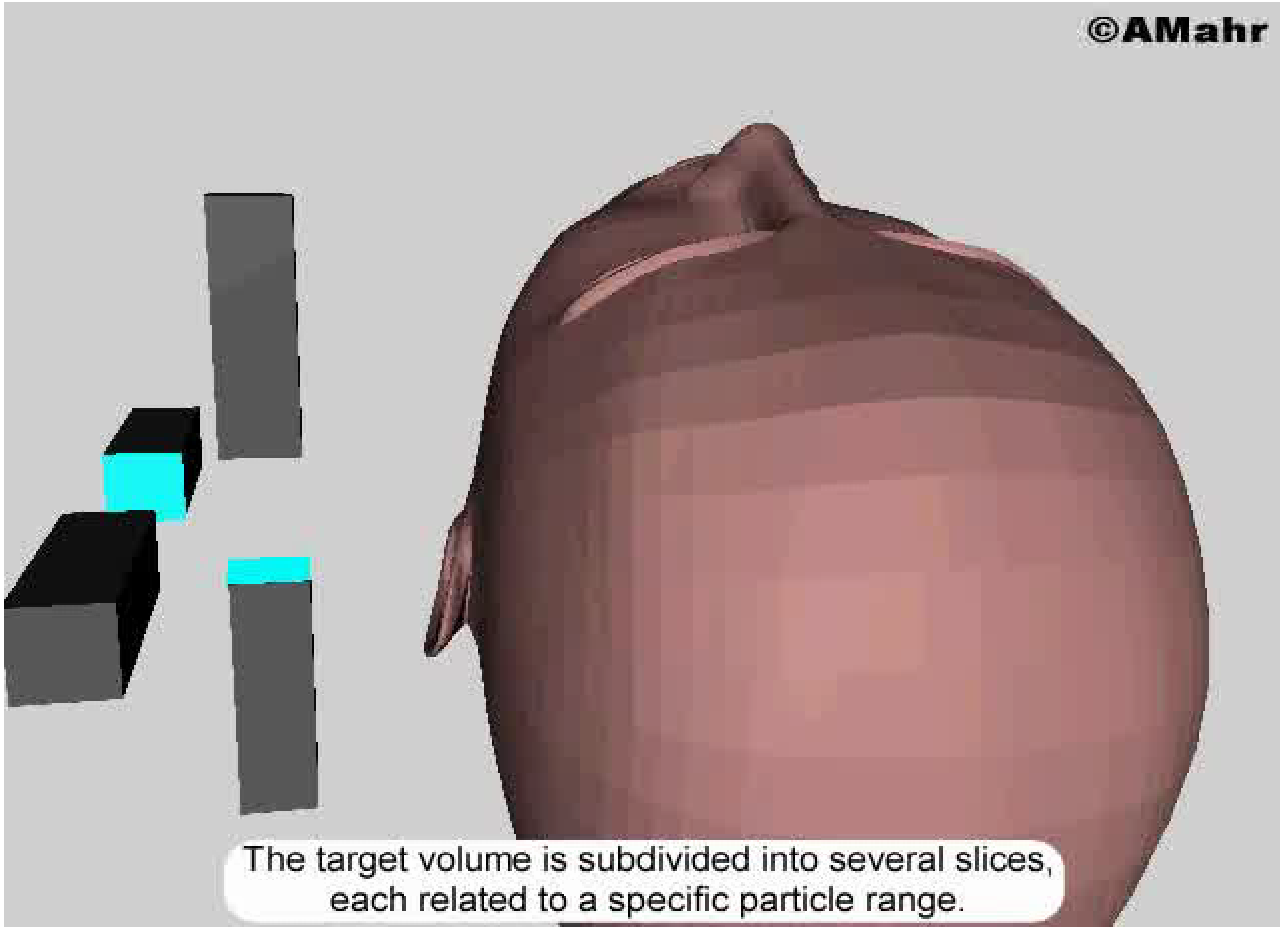
Ridge filter design and SOBP for HIMAC



Physical depth dose   Biological effective dose

3D Active beam scanning at GSI

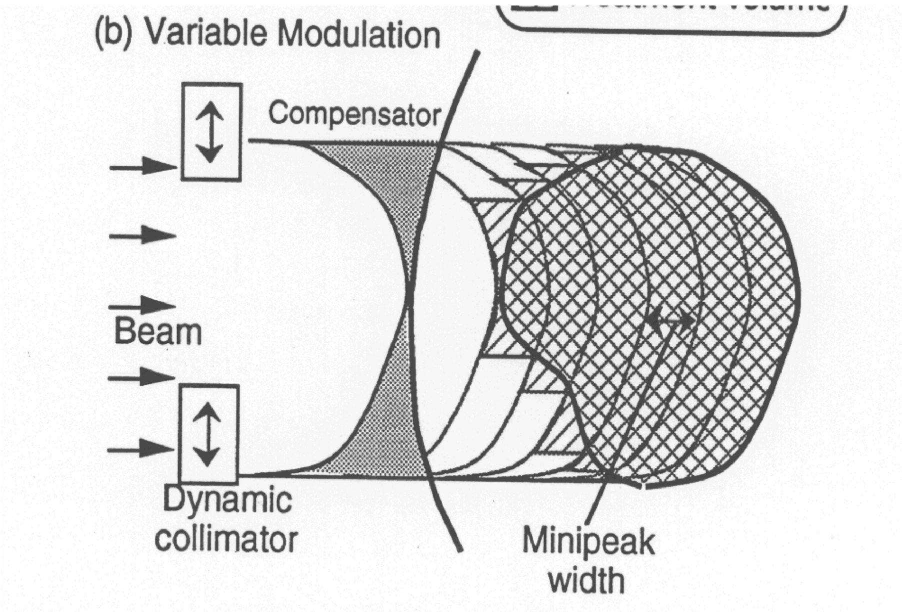
- Energy variation of synchrotron (~1mm resolution depth)
- Intensity controlled raster scanning (~2 mm, 5mm fwhm)

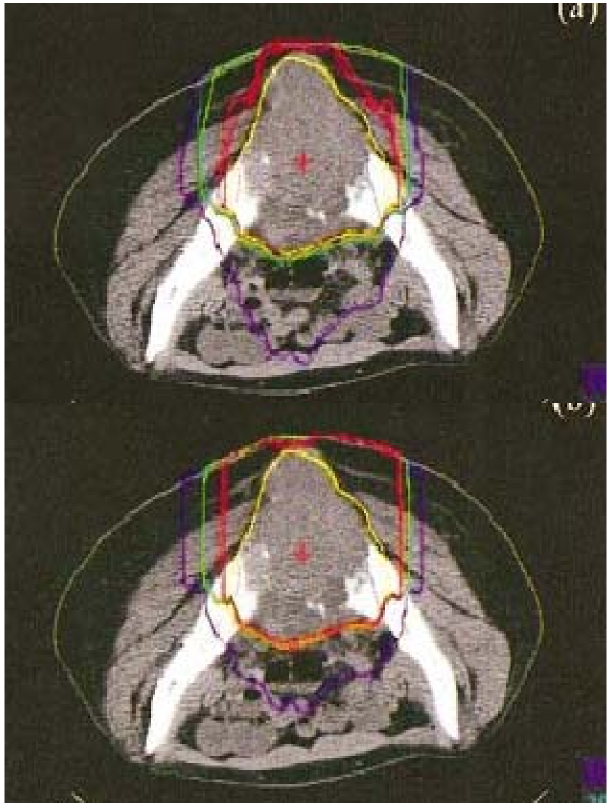


Optimization if typically 30-50 energies, 20 000 -50 000 field spots

3D active beam shaping (protons: PSI, ions: GSI)

- No patient specific hardware
- Fragmentation model needed
- Biological modelling needed



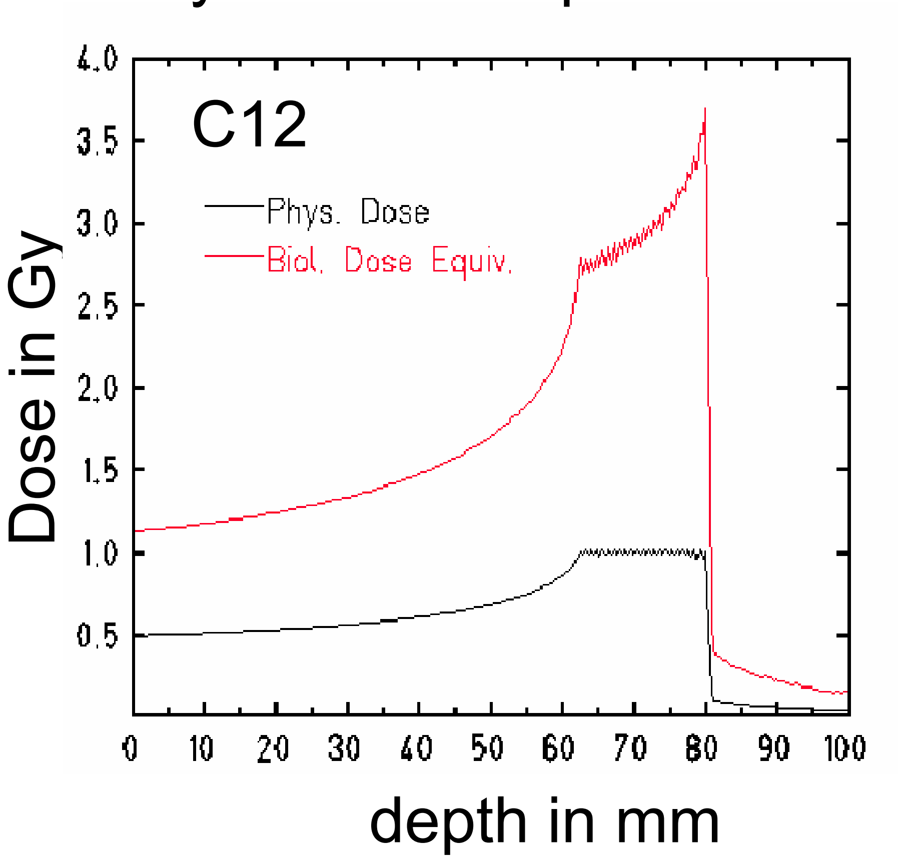


Single Bragg peaks
Variable energy
Scanning or MLC

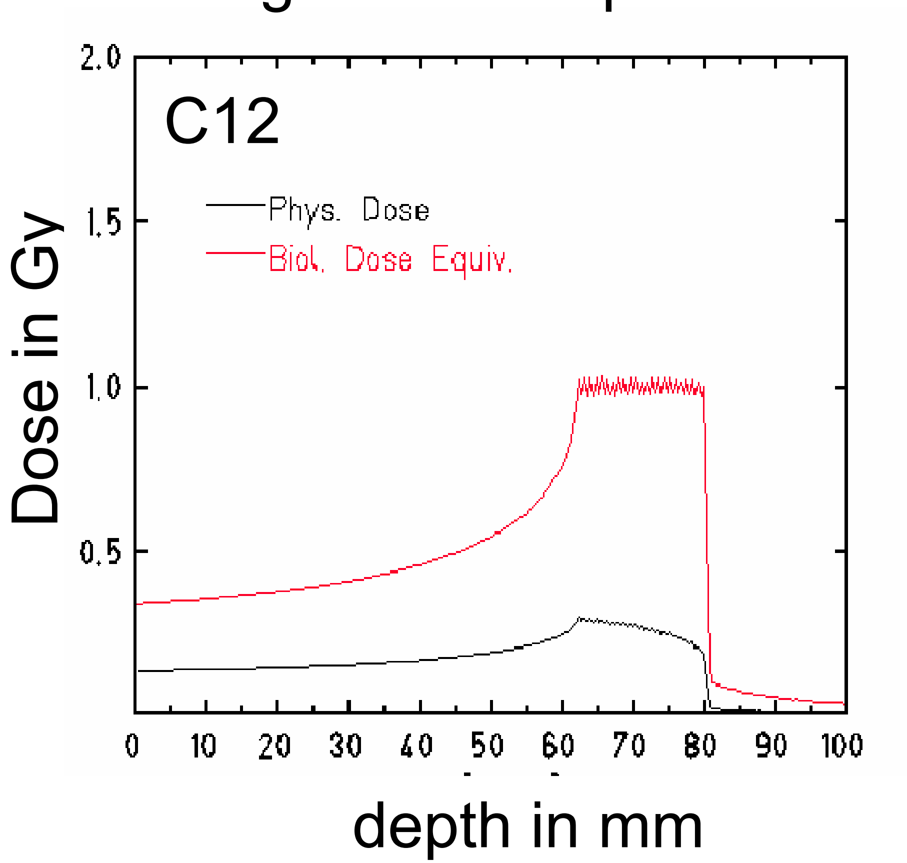
Dose conformation also at proximal end

Calculation of biological effective dose (ions)

Physical dose optimization



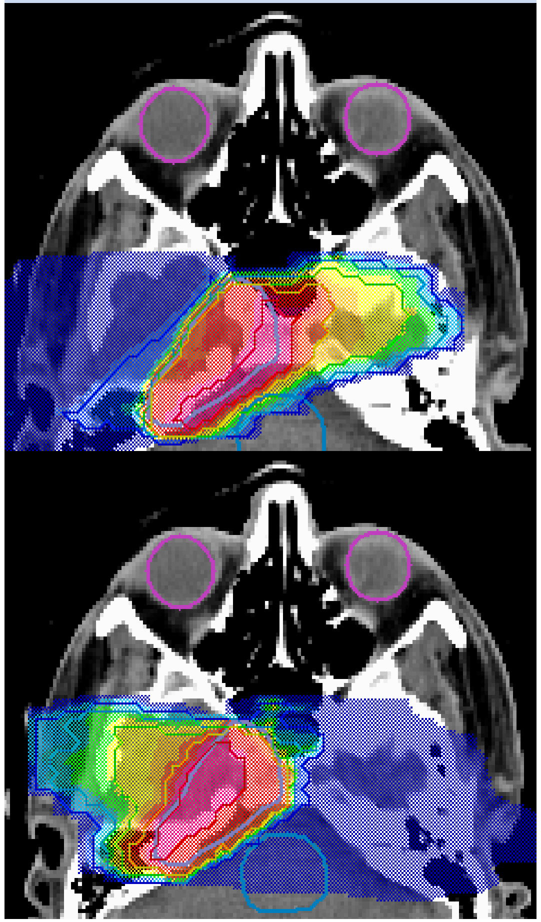
Biological dose optimization



- Account for nuclear fragmentation in every point in 3D
- Detailled biological modelling necessary

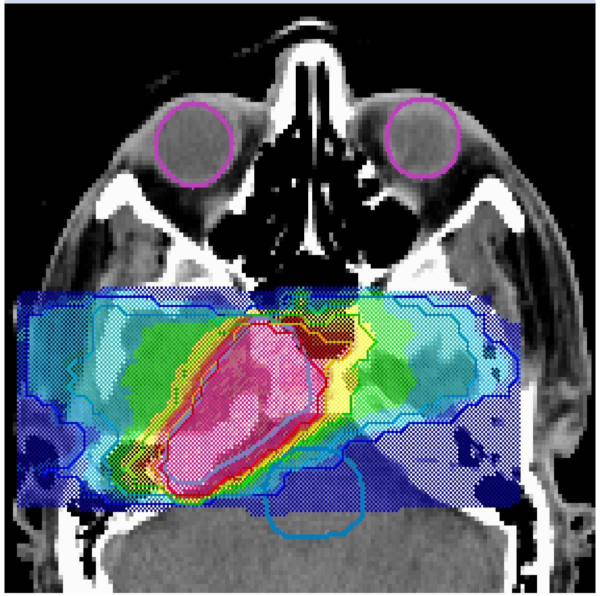
Biological treatment planning for carbon ions

Physical dose
of single fields

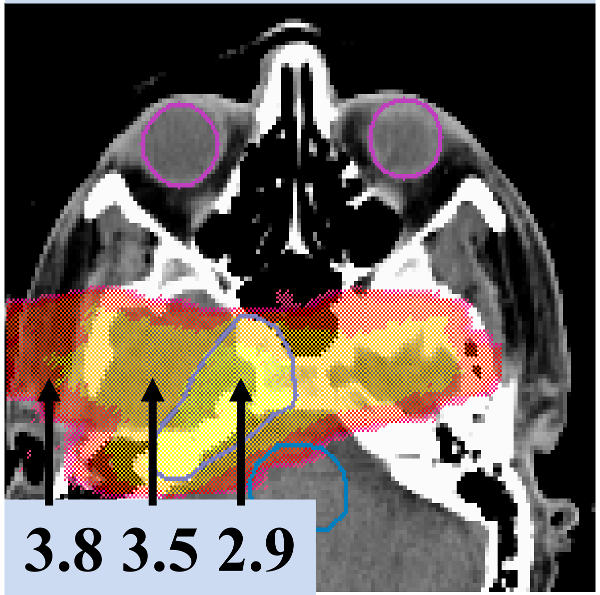


Local effect model of Scholz and Kraft:
Calculation of RBE as a 3D distribution
Input: X-ray survival curves &
fragmentation spectra

Biological effective dose

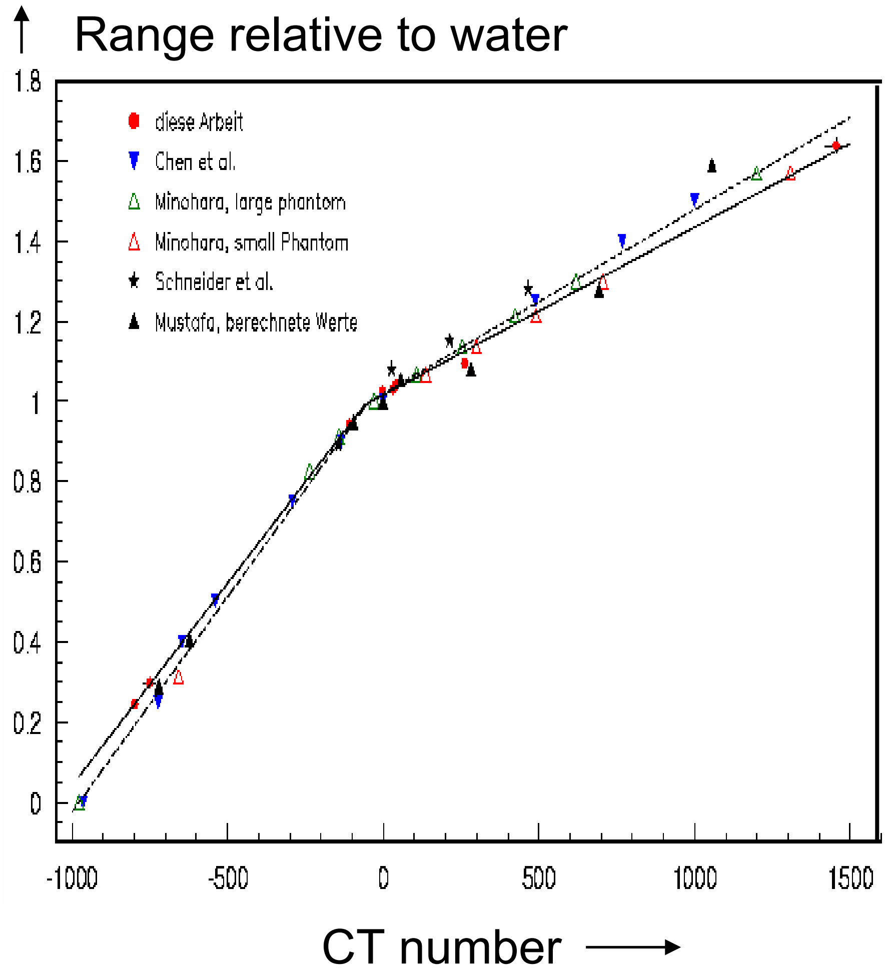


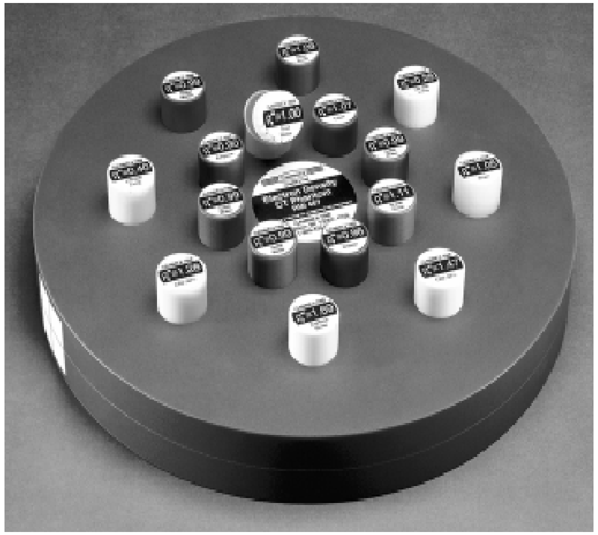
RBE-distribution

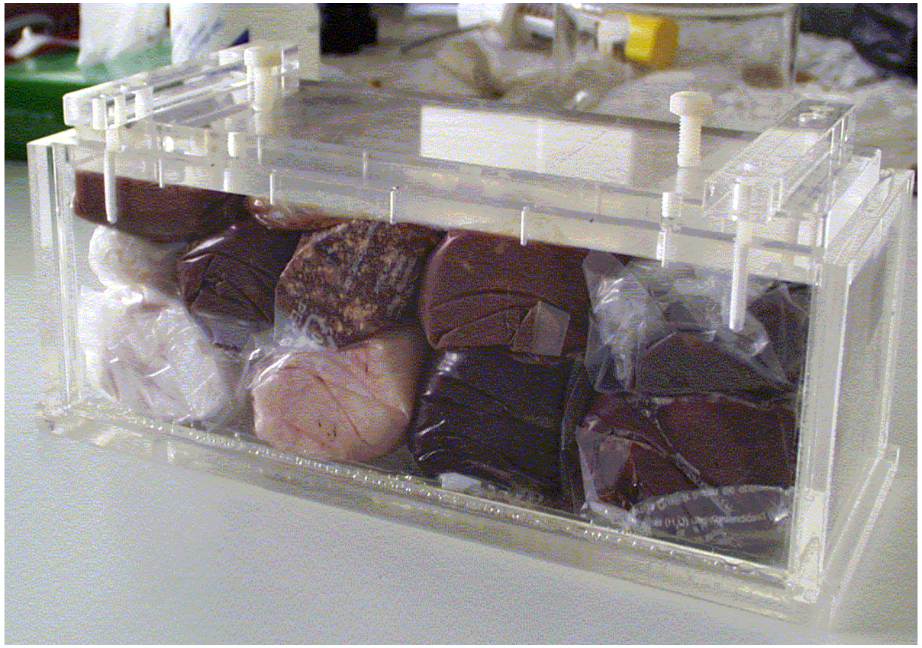


Empirical range calculation from CT numbers

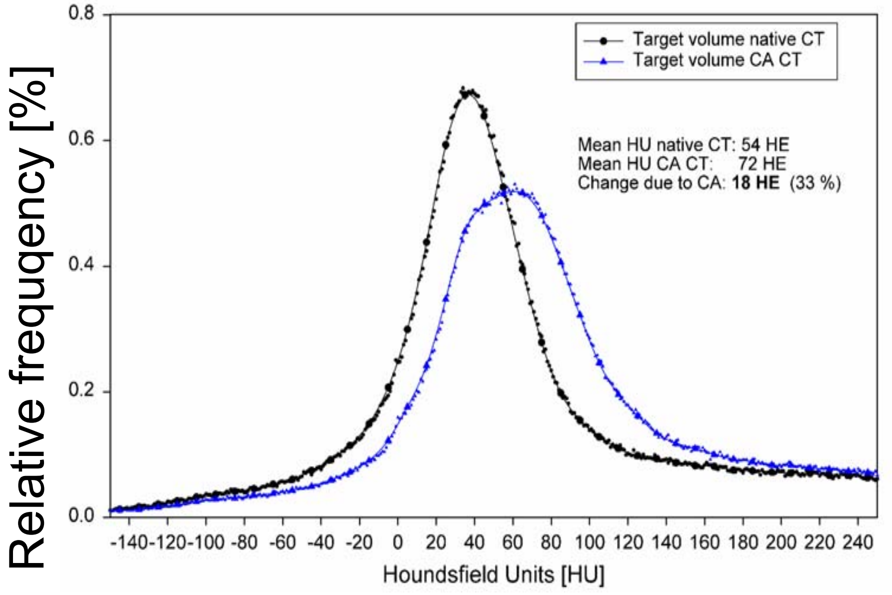
- Tissue equivalent phantoms
- Real tissue measurements

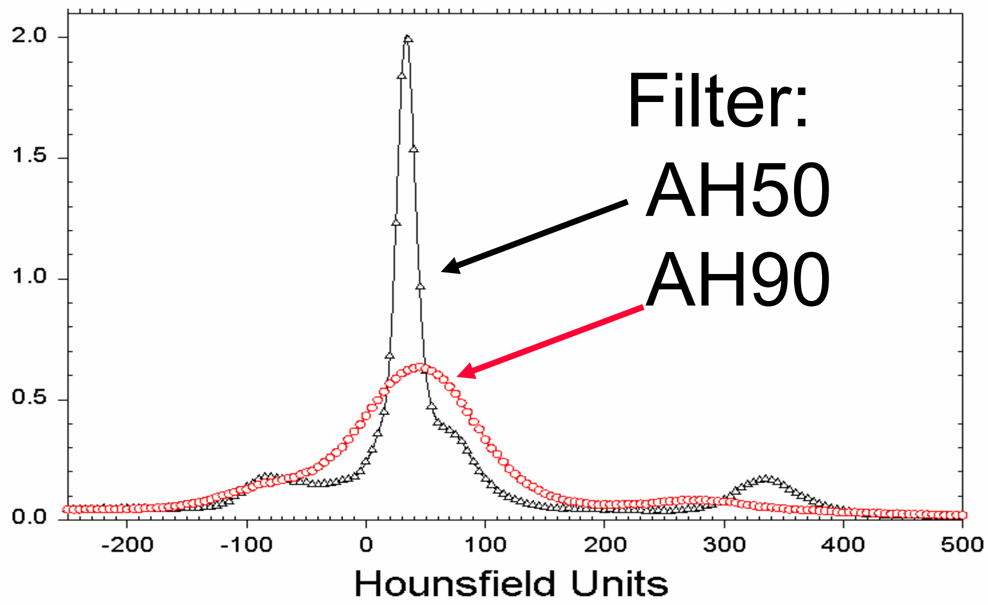






Possible distortions of CT numbers





Contrast agent in CT

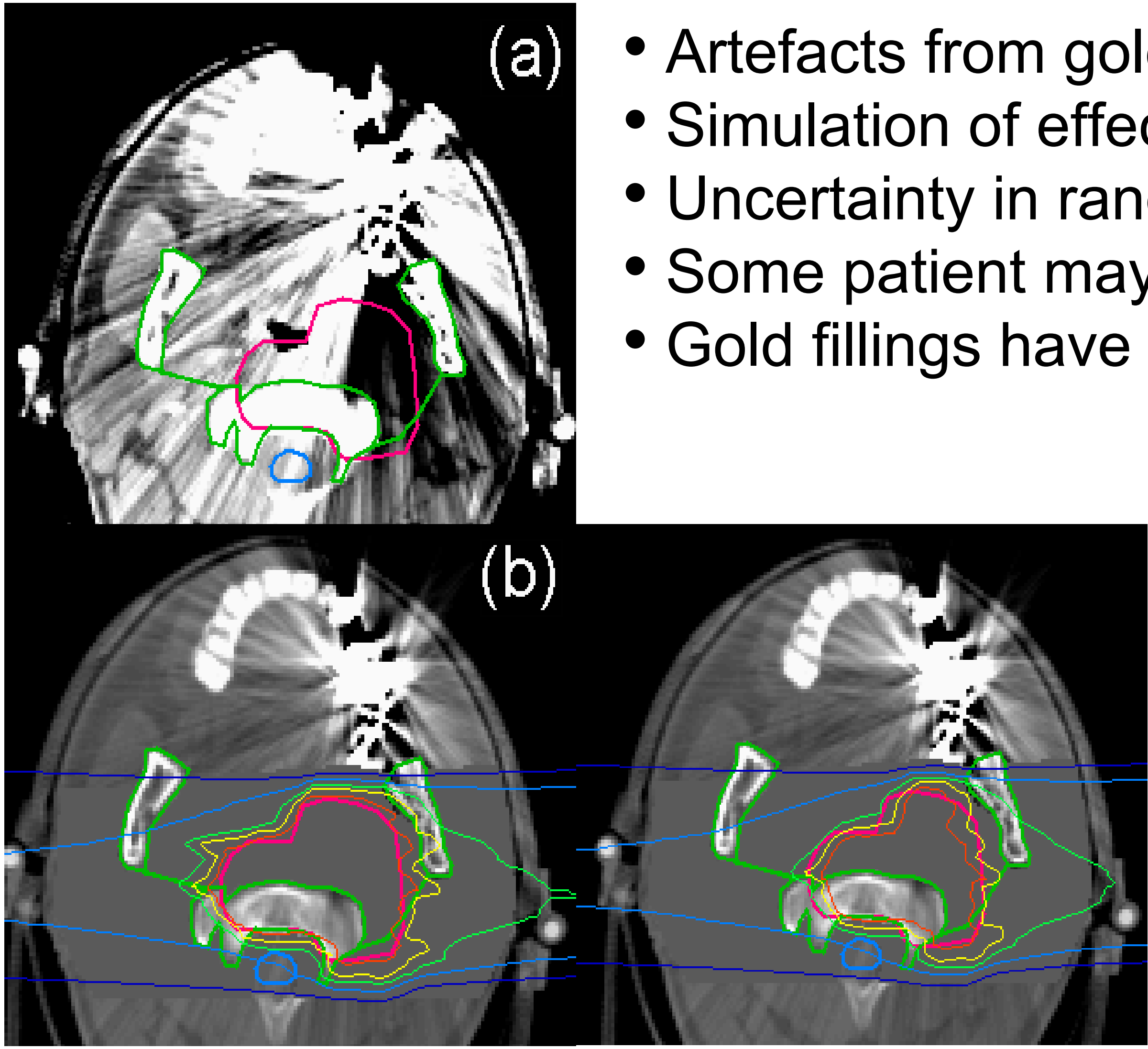
- mean shift (25 pat.): 18 HU
- max shifts: 36 HU
- Errors in range < 1.6 %

Reconstruction filters

- redistribution of HU numbers
- Errors in range < 3 %

Special attention to QA of the CT and imaging protocols !

Metal artifacts in CT images

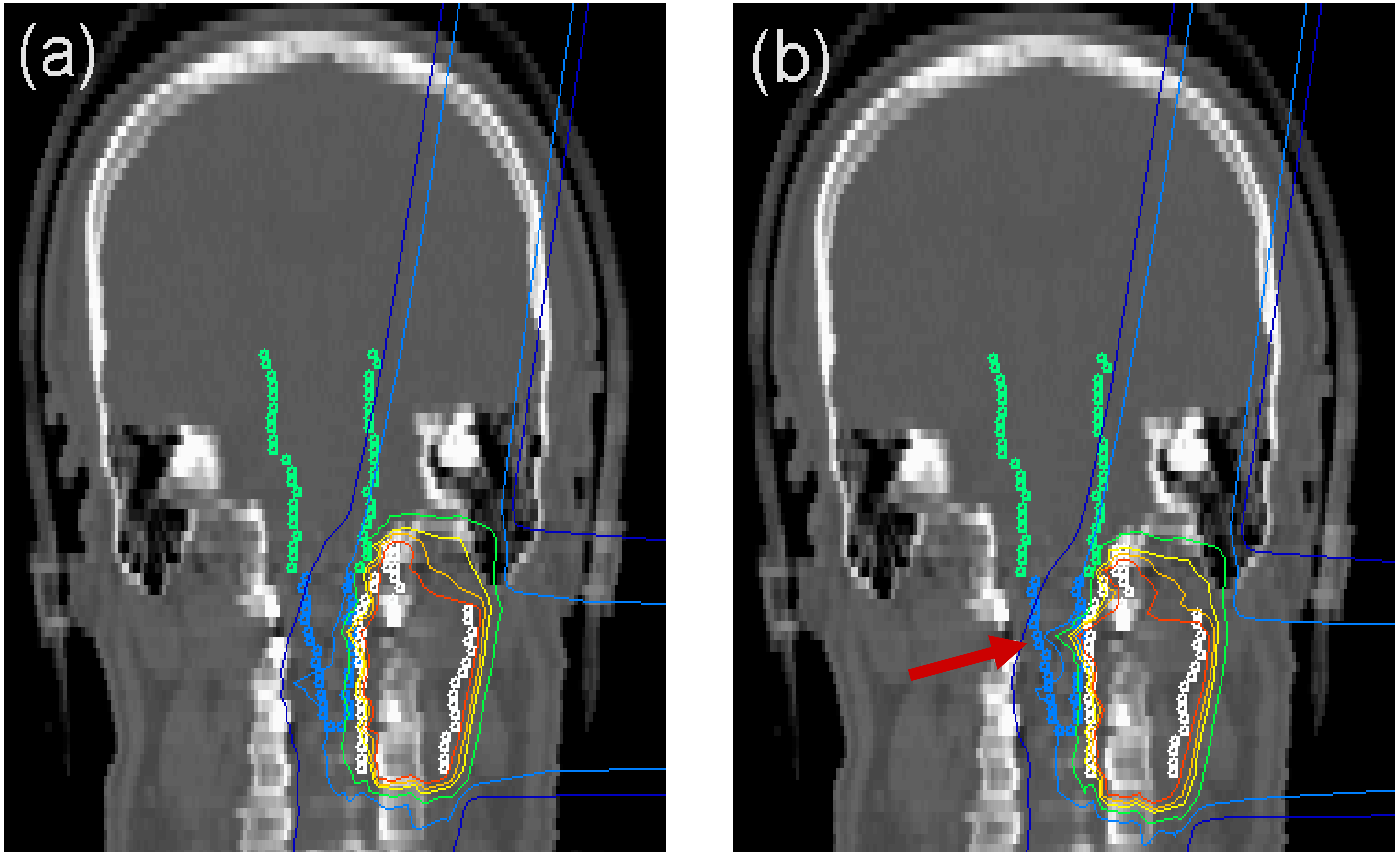


- Artefacts from gold fillings or implants
- Simulation of effects of wrong HU
- Uncertainty in range calculation
- Some patient may be rejected
- Gold fillings have to be removed

Uncertainties in Range due to misalignment

Wrong patient position changes the tissue traversed by the beam and may lead to over/underdosages:

Effect of a 5mm cranial shift on the particle ranges:



The robustness of treatment plans has to be tested!

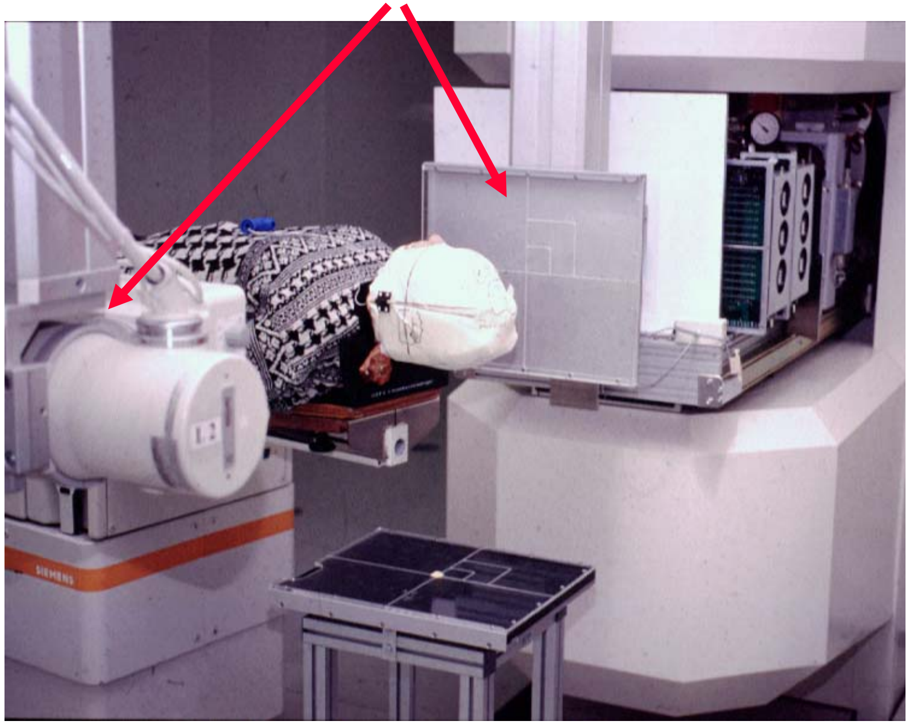
Patient setup and treatment at GSI

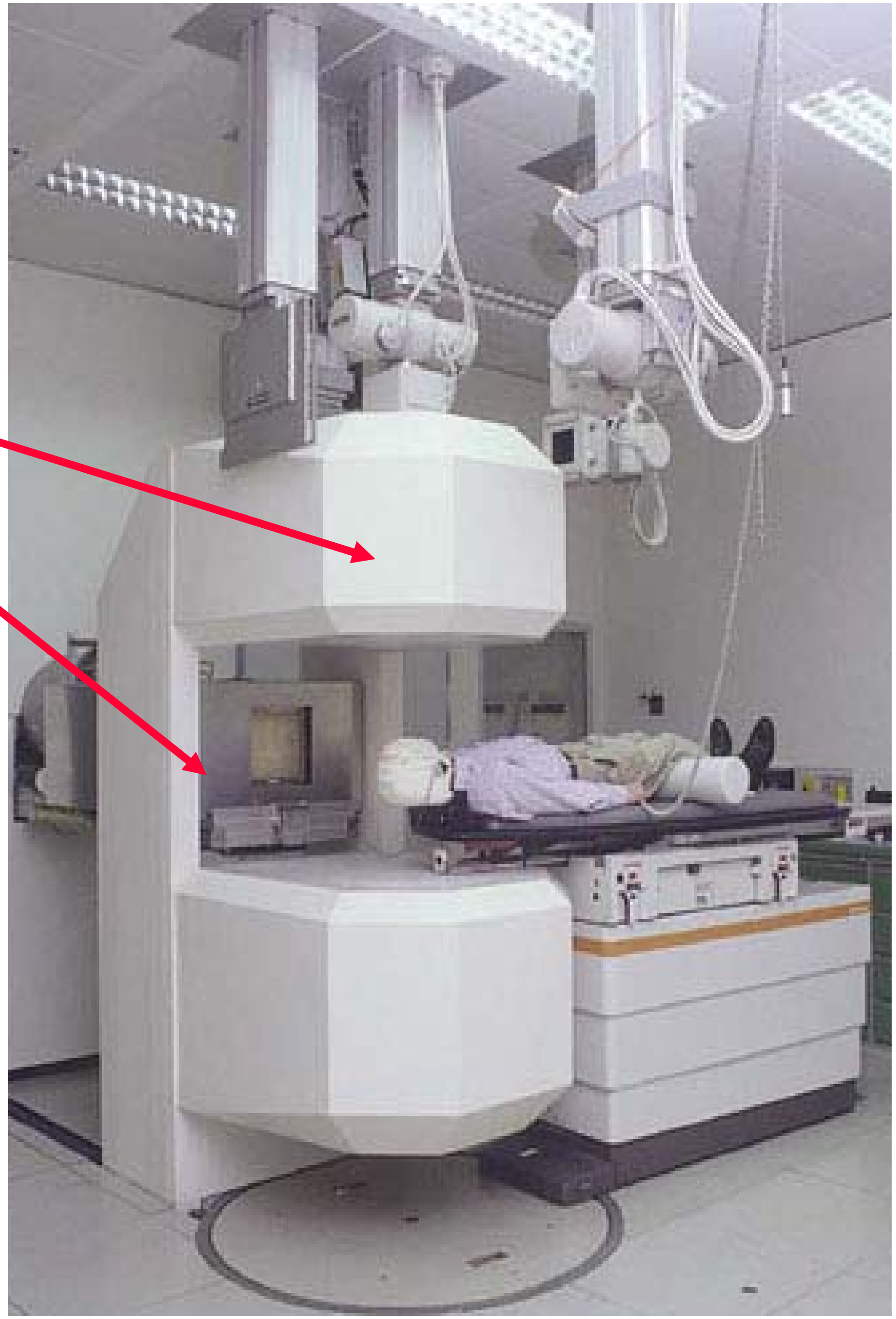
Fixed beamlines, no gantry

PET-camera

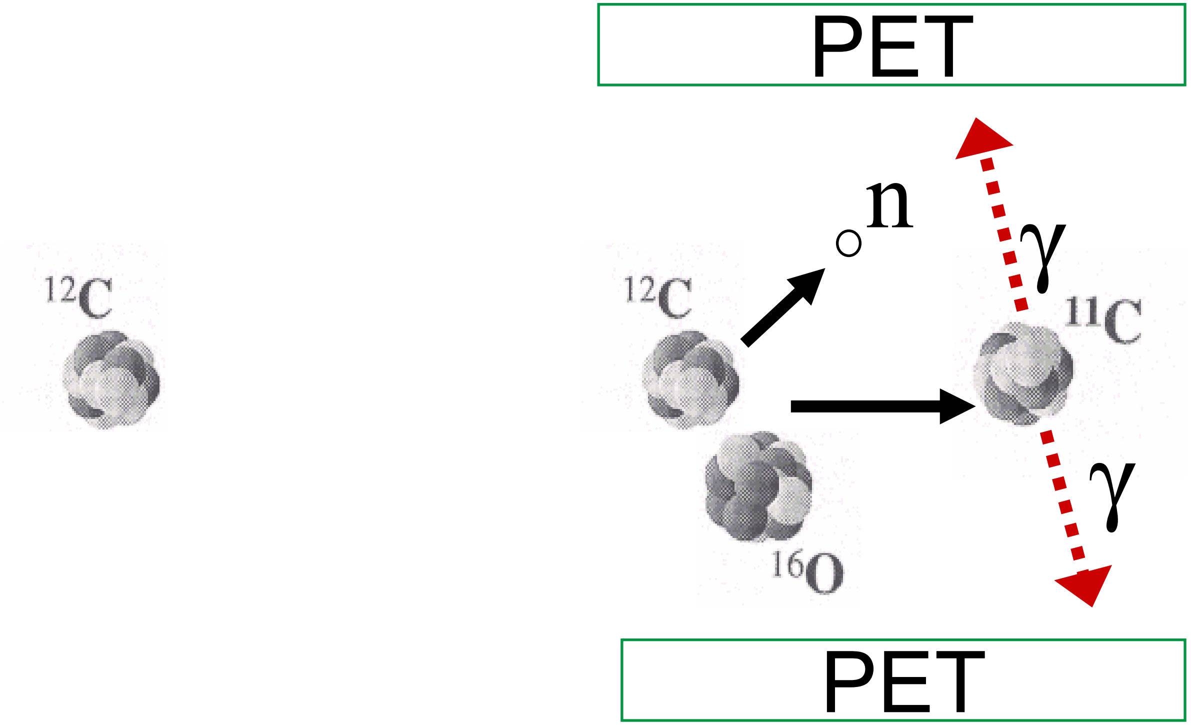
X-ray system

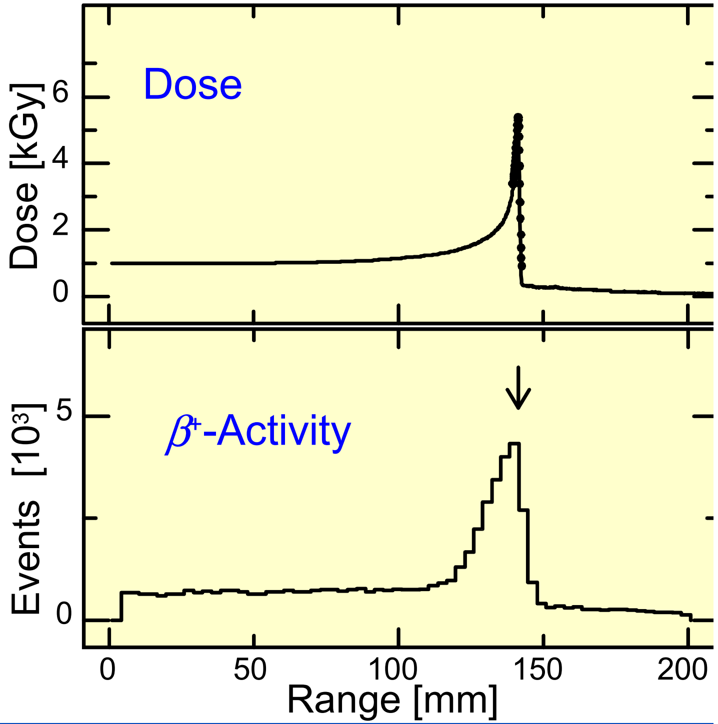
Beam line





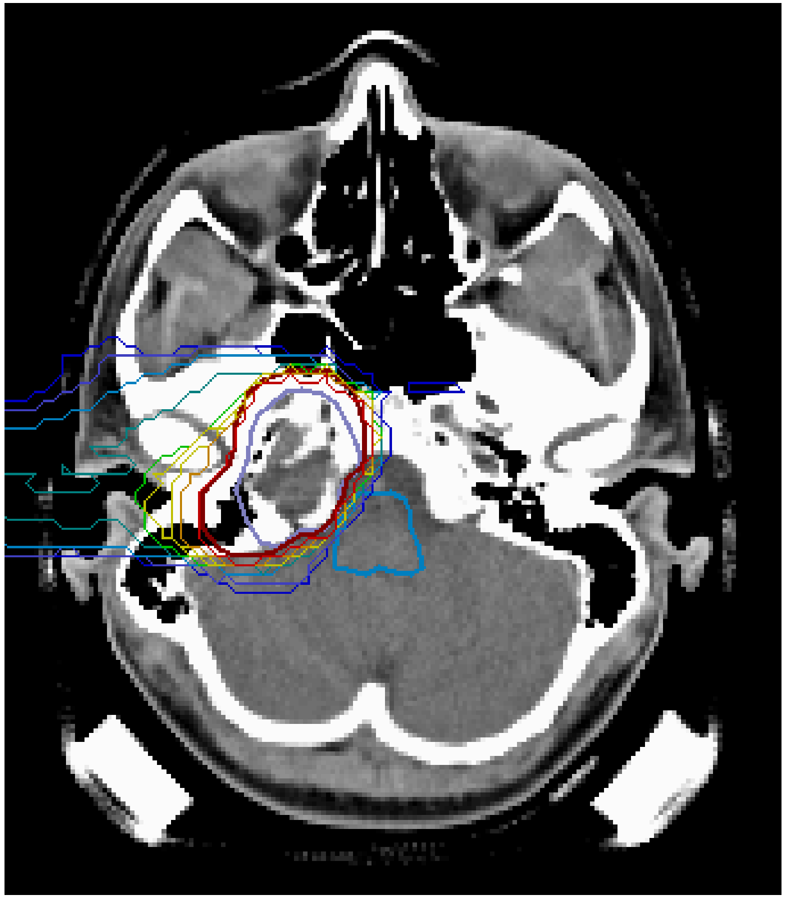
In vivo monitoring with PET for ions



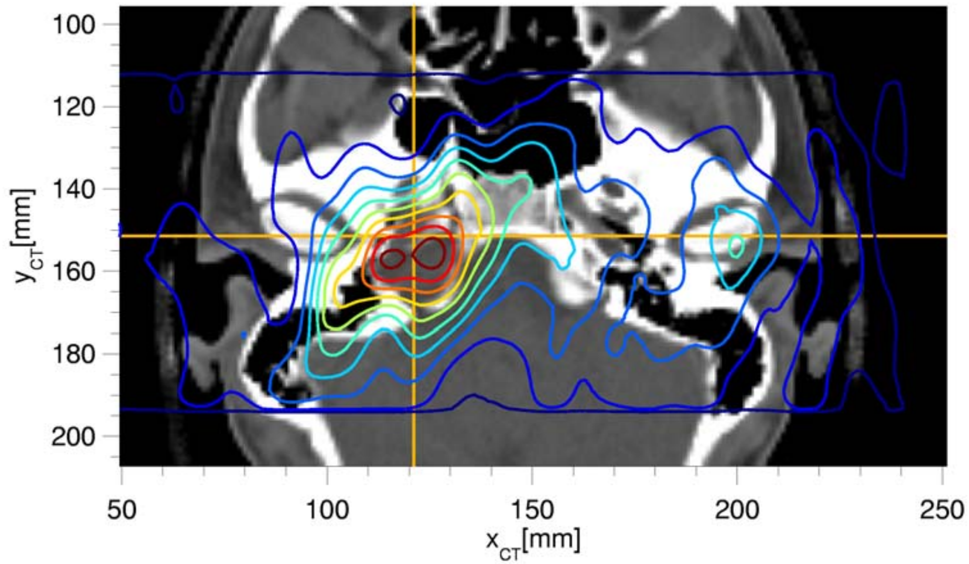


- Import of PET activity into TPS
- Comparison with calculated activity

PET – Monitoring in situ
Patient with Chondrosarcoma of skull base



Dose distribution carbon ions

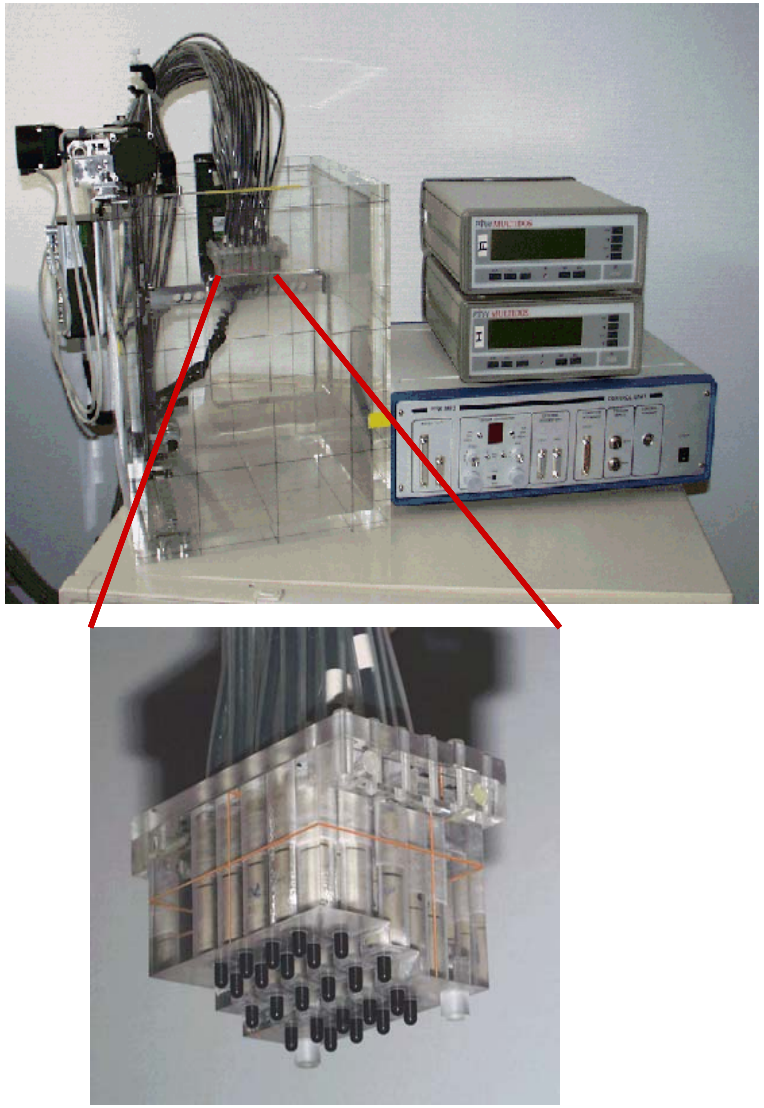


PET-Measurement

Dose verification for active beam delivery

Problem:

- Scanning chambers for dynamic fields not suitable
- Simulateous measurement of many channels



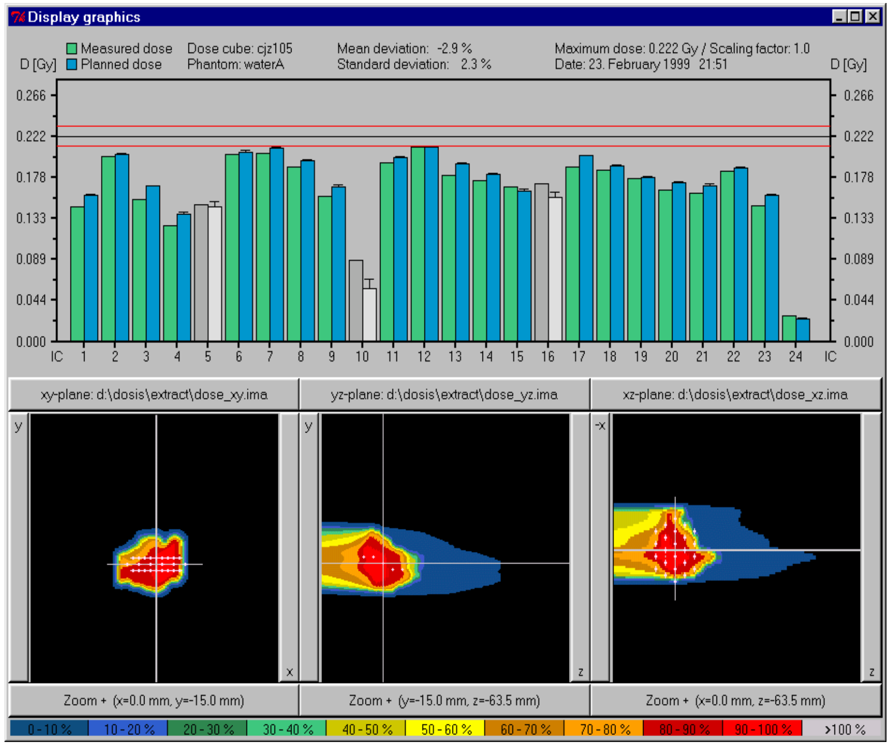
Verification phantom:

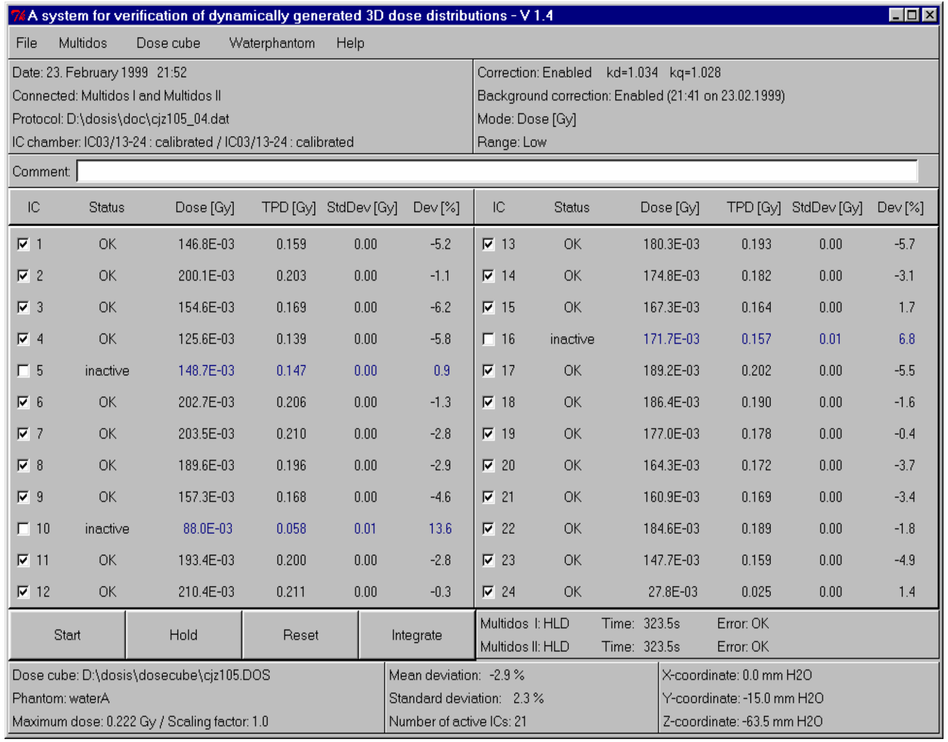
- 24 Pinpoint chambers
- Readout by 2 Multidos-Dosemeters
- Computer controlled movement of the chambers in the water phantom

Verification software

- Interface to therapy planning
- Display dose in water
- Display of chamber positions

- Measurement at 24 positions
- Comparison w. therapy planning
- Analysis and documentation





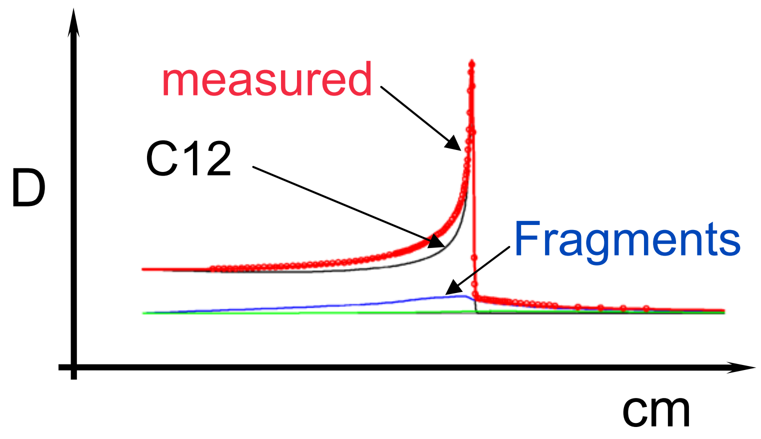
IC	Status	Dose [Gy]	TPD [Gy]	StdDev [Gy]	Dev [%]	IC	Status	Dose [Gy]	TPD [Gy]	StdDev [Gy]	Dev [%]
1	OK	146.8E-03	0.159	0.00	-5.2	13	OK	180.3E-03	0.193	0.00	-5.7
2	OK	200.1E-03	0.203	0.00	-1.1	14	OK	174.8E-03	0.182	0.00	-3.1
3	OK	154.6E-03	0.169	0.00	-6.2	15	OK	167.3E-03	0.164	0.00	1.7
4	OK	125.6E-03	0.139	0.00	-5.8	16	inactive	171.7E-03	0.157	0.01	6.8
5	inactive	148.7E-03	0.147	0.00	0.9	17	OK	189.2E-03	0.202	0.00	-5.5
6	OK	202.7E-03	0.206	0.00	-1.3	18	OK	186.4E-03	0.190	0.00	-1.6
7	OK	203.5E-03	0.210	0.00	-2.8	19	OK	177.0E-03	0.178	0.00	-0.4
8	OK	189.6E-03	0.196	0.00	-2.9	20	OK	164.3E-03	0.172	0.00	-3.7
9	OK	157.3E-03	0.168	0.00	-4.6	21	OK	160.9E-03	0.169	0.00	-3.4
10	inactive	88.0E-03	0.058	0.01	13.6	22	OK	184.6E-03	0.189	0.00	-1.8
11	OK	193.4E-03	0.200	0.00	-2.8	23	OK	147.7E-03	0.159	0.00	-4.9
12	OK	210.4E-03	0.211	0.00	-0.3	24	OK	27.8E-03	0.025	0.00	1.4

Verification of therapy plans prior to first application

Carbon Ion Dose Determination

$k_{Q,Qo}$ concept of IAEA TRS-398

$$k_{Q,Q_o} = \frac{\left(\frac{w_{air}}{e}\right)^{^{12}C}}{\left(\frac{w_{air}}{e}\right)^{^{60}Co}} \cdot \frac{\bar{s}_{w,air}^{\,^{12}C}}{\left(\bar{L}/\rho\right)_{w,air}^{^{60}Co}} \cdot \frac{p^{^{12}C}}{p^{^{60}Co}}$$

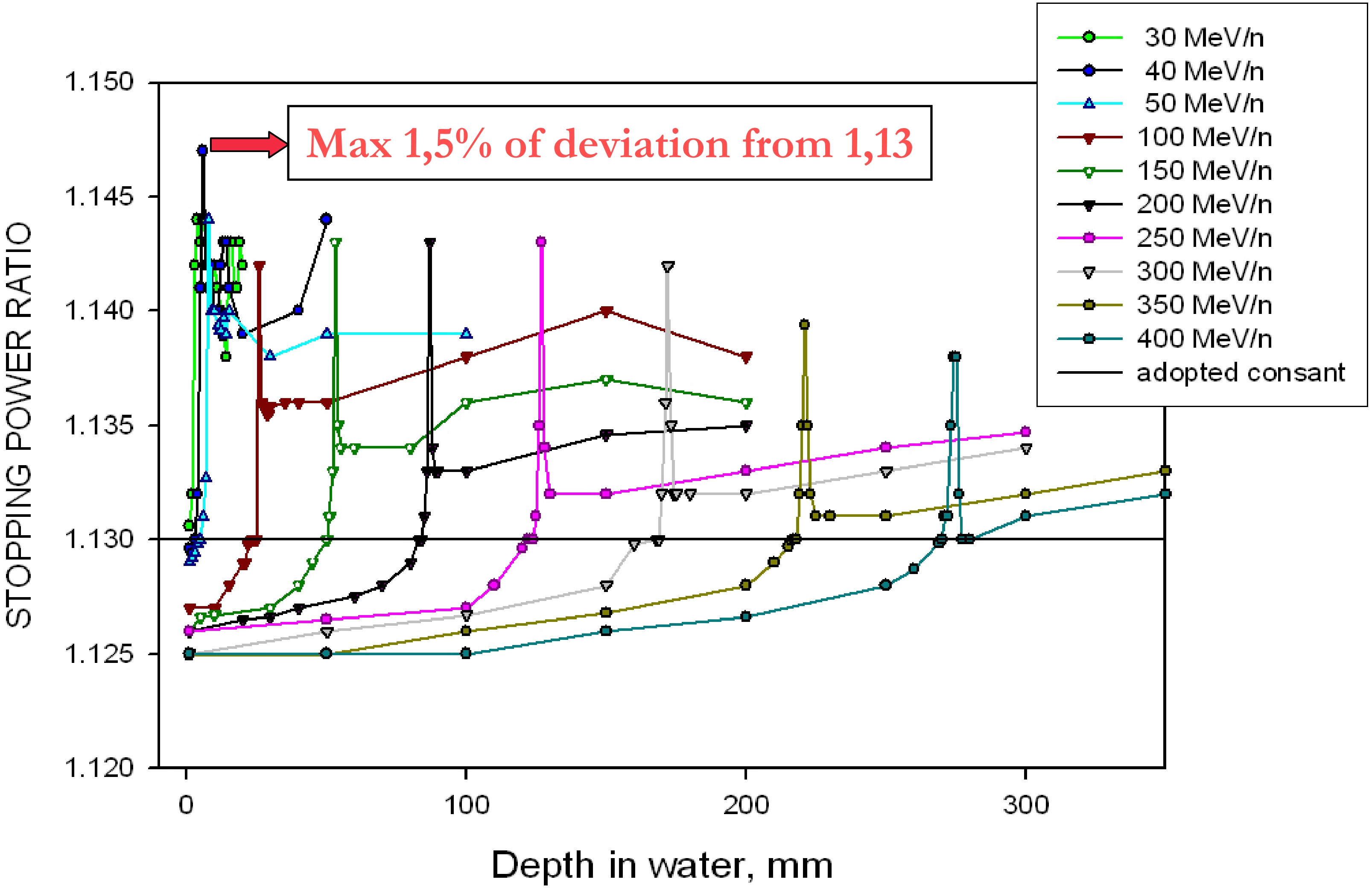


Spencer-Attix Stopping Power Ratio

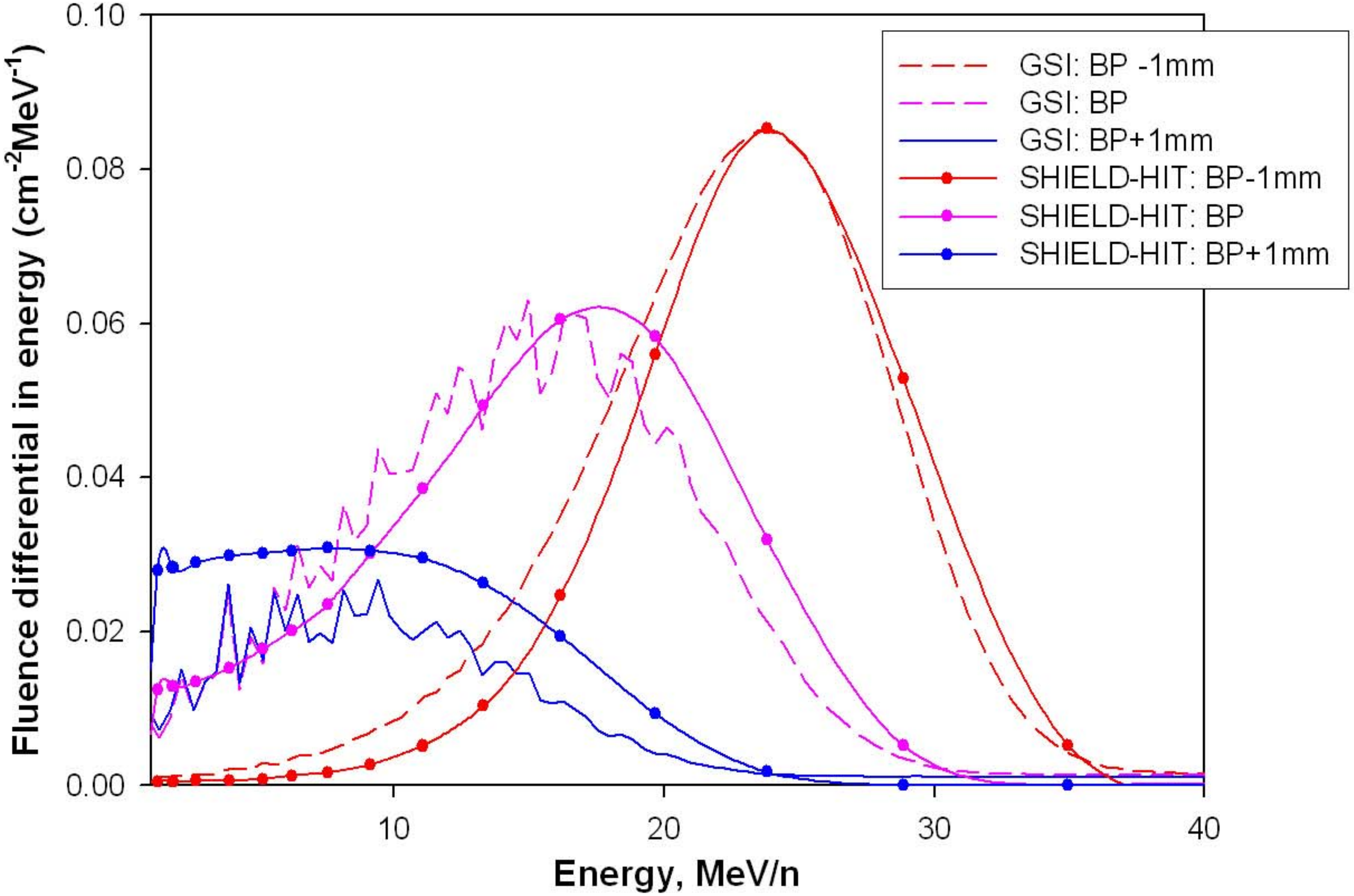
$$\bar{s}_{w,air} = \frac{\sum_i \int_0^\infty \Phi_{E,i} (S_i(E)/\rho)_w \, dE}{\sum_i \int_0^\infty \Phi_{E,i} (S_i(E)/\rho)_{air} \, dE}$$

Parameter	$(w/e)^{^{12}C}$	$(w/e)^{^{60}Co}$	$s_{w,air}^{^{12}C}$	$(\bar{L}/\rho)_{w,air}^{^{60}Co}$	$p^{^{60}Co}$	$p^{^{12}C}$
Uncertainty	**1.5 - 4%**	**0.2%**	**2.0%**	**0.5%**	**0.6%**	**1%?**

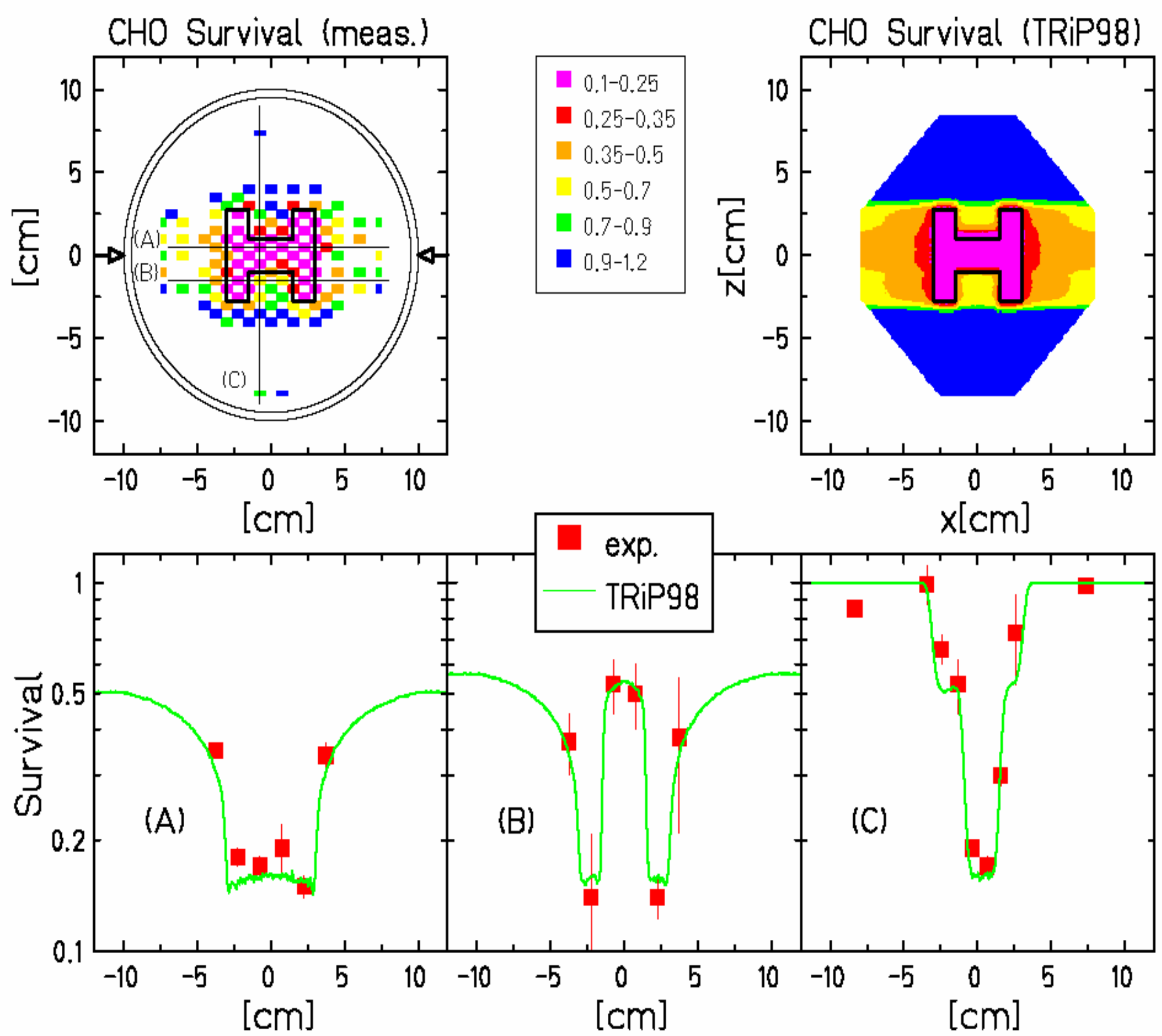
Stopping power ratio water/air for C12 averaged over fragment spectrum



Energy spectrum of a 360 MeV/u C12 in water close to Bragg peak (Monte Carlo)



Biological Verification



- Biological planning and optimization for CHO Zellen
- Calculation of cell survival
- Irradiation of stack with probes of cells
- every time consuming

Krämer et al.
Phys Med Biol.
48: 2063-70,
2003

Application in clinical studies at GSI

Skull base chordoma and chondrosarcoma

Fully fractionated therapy, 60 Gye in 20 fractions
8/98 - 12/01: 67 patients treated in phase I/II studies
since 3/02: approval to use HIRT as standard therapy (~55 pat.)

Adenoidcystic Carcinoma and atypical meningeoma

Carbon ion boost after conventional therapy or IMRT
18 Gye in 6 fractions HI + 54 Gy photons
3/00 - 8/04: ~45 patients in phase I/II studies

Pelvic and spinal chordoma and chondrosarcoma

Carbon ion boost after conventional therapy or IMRT
18 Gye in 6 fractions HI + 54 Gy photons
6/00 - 8/04: ~22 patients in phase I/II studies

Clinical Outcome of patient treatments @ GSI Status 2 / 2003

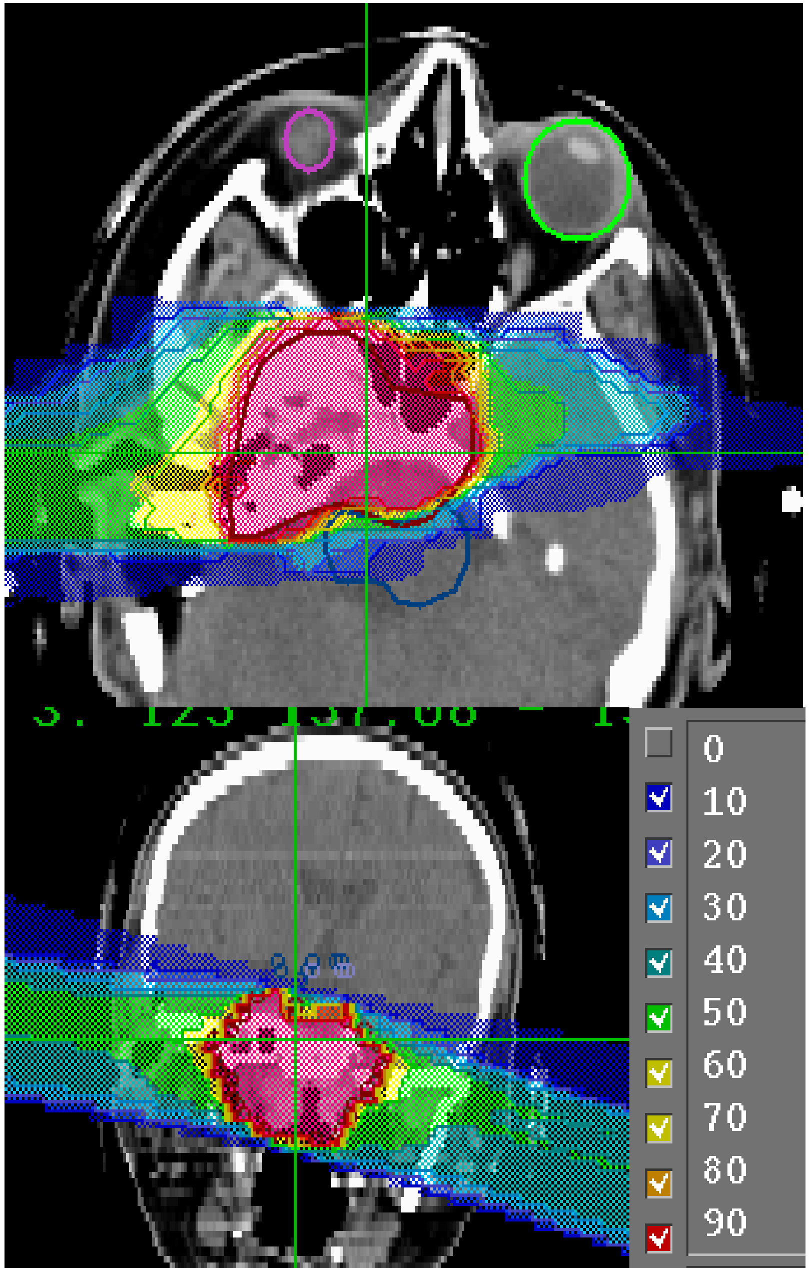
Indication	#	follow-up	act. LC	3y Surv.	Side effects
Chord. SB	54	20m	81% (3y)	91%	<= 3° CTC
Ch.sarc. SB	33	20m	100% (3y)		<= 3° CTC
Sacral Chord.	8	~22m	7(8) pat.	7(8)	none
Cervical Ch/CS	9	~22m	8(9) pat.	8(9)	<= 3° CTC
ACCa	21	14m	62%(3y)	75%	<= 3° CTC

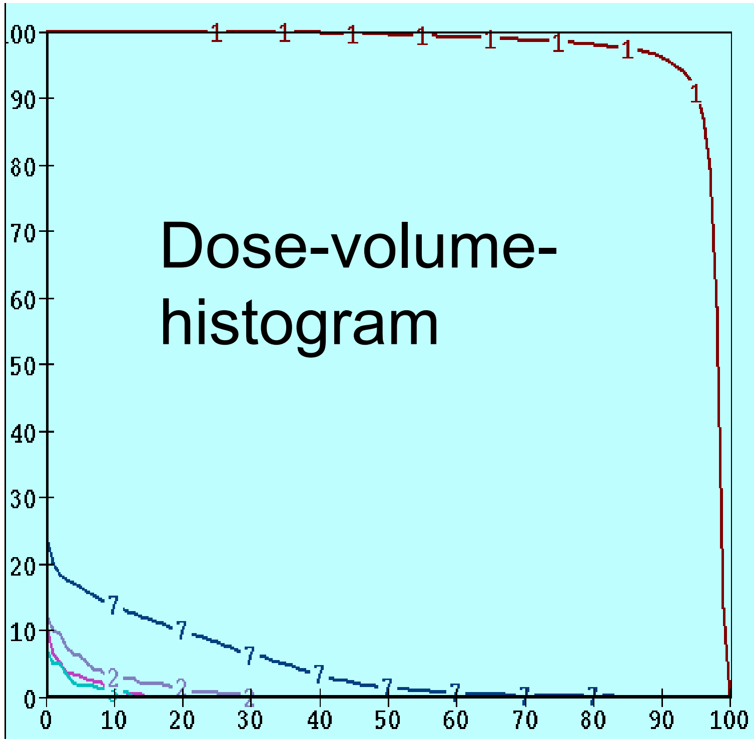
- Outcome for ACC: 75% vs. 24% after Photon IMRT, while severe side effects (< °2 CTC) are < 5% (vs >10% for neutron RT) !

- No severe late effects (>2° CTC) of spinal chord were observed

- ~ 30 patients treated outside protocols (palliative, re-irradiation)

Clinical application: Skull base tumor

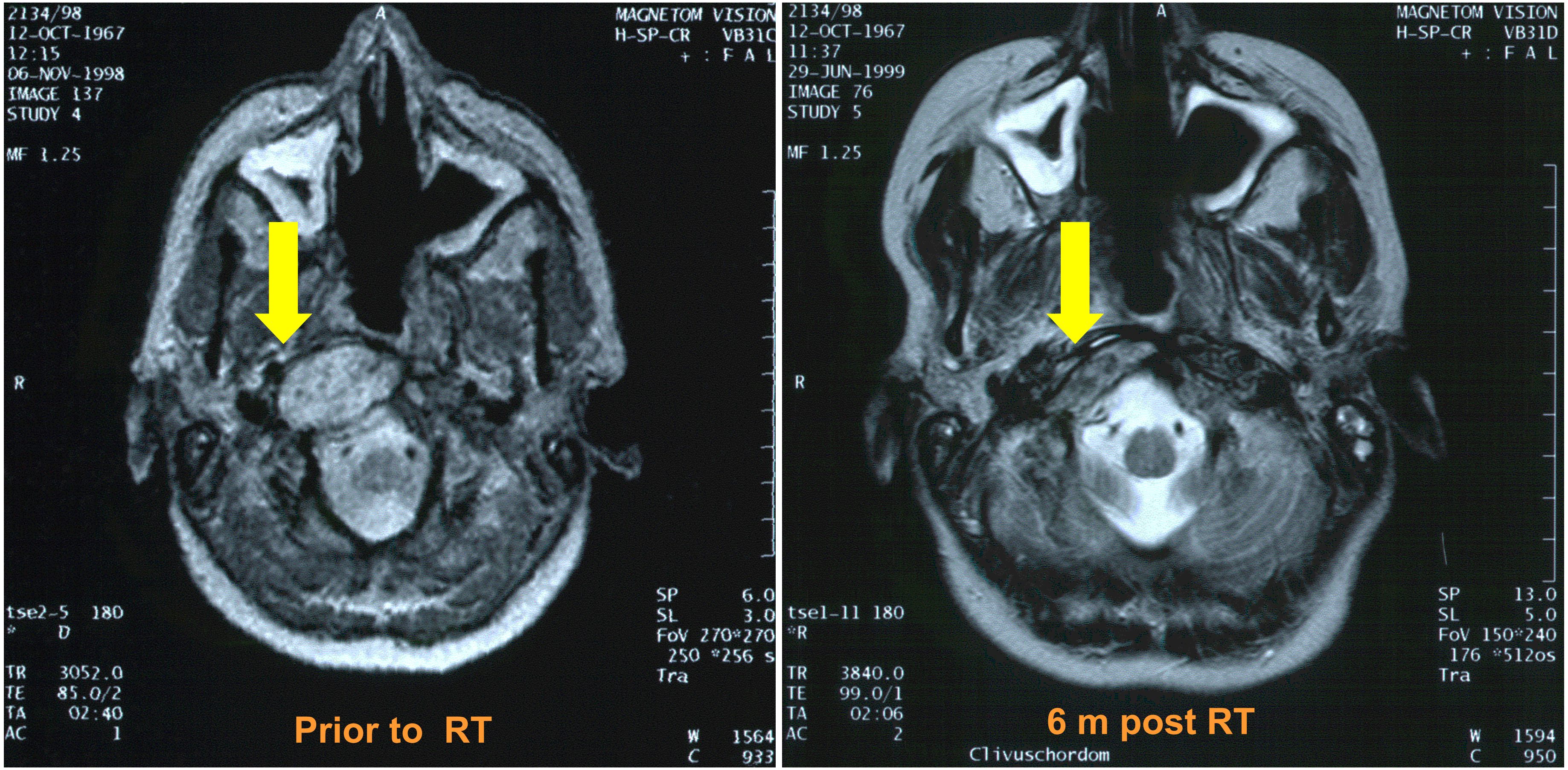




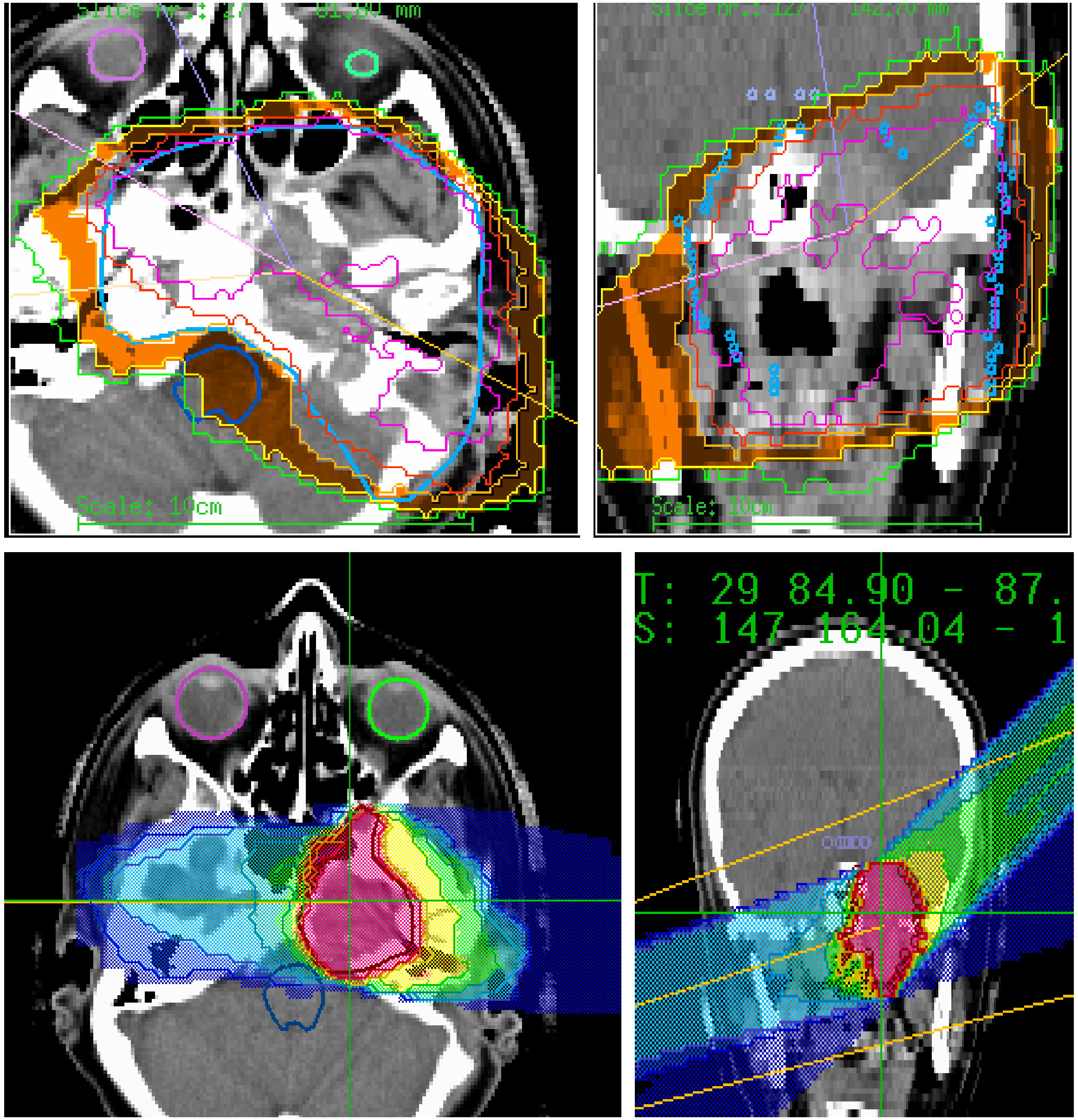
Primary Iontherapy
2 Fields
60 Gye in 20 Fractions

Example: Recurrent Clivuschordoma

- subtotal resection 1996
- proton therapy 79.2GyE,1996
- 11/98 20.8 Gy FSRT + 27 GyE C12 at recurrency



Combination Therapy for Adenoidcystic Ca.

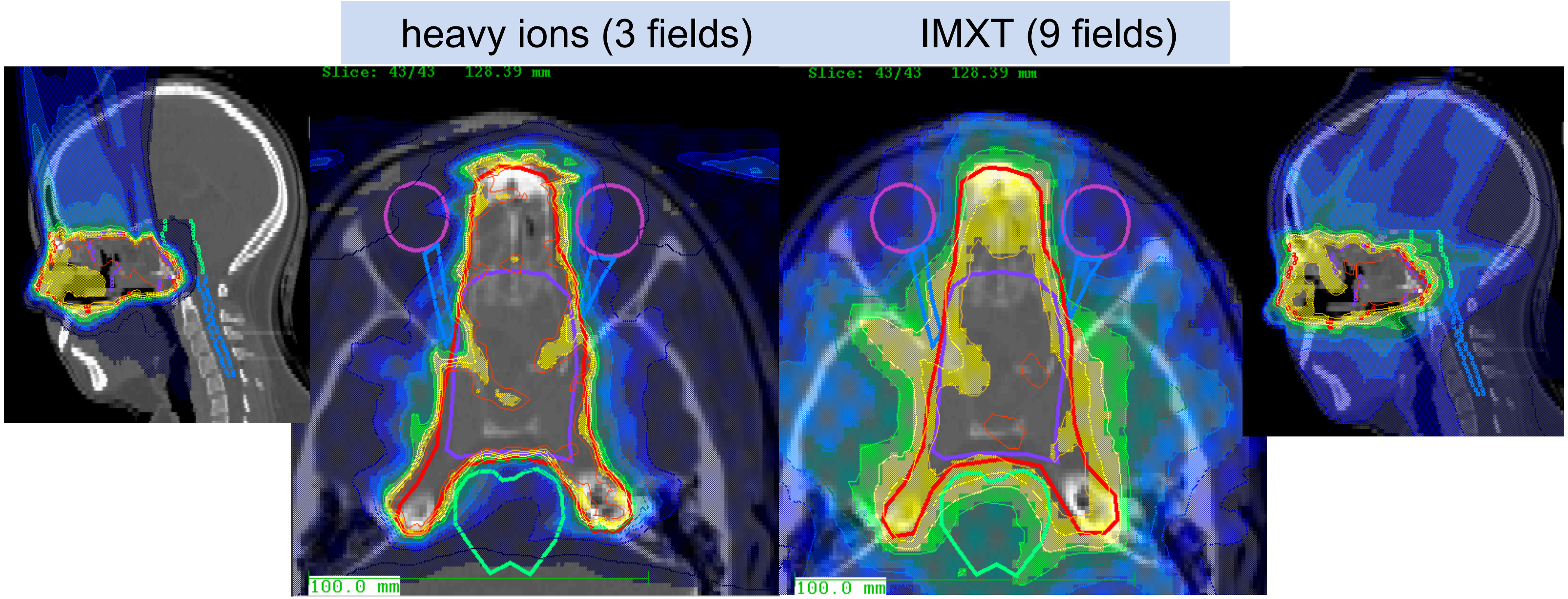


Fractionated radiotherapy with photons to 54 Gy to PTV

Boost treatment with carbon ions 18 Gy to GTV

Rationale:
- Normal tissue in PTV
- More robust plans
- More patients treated

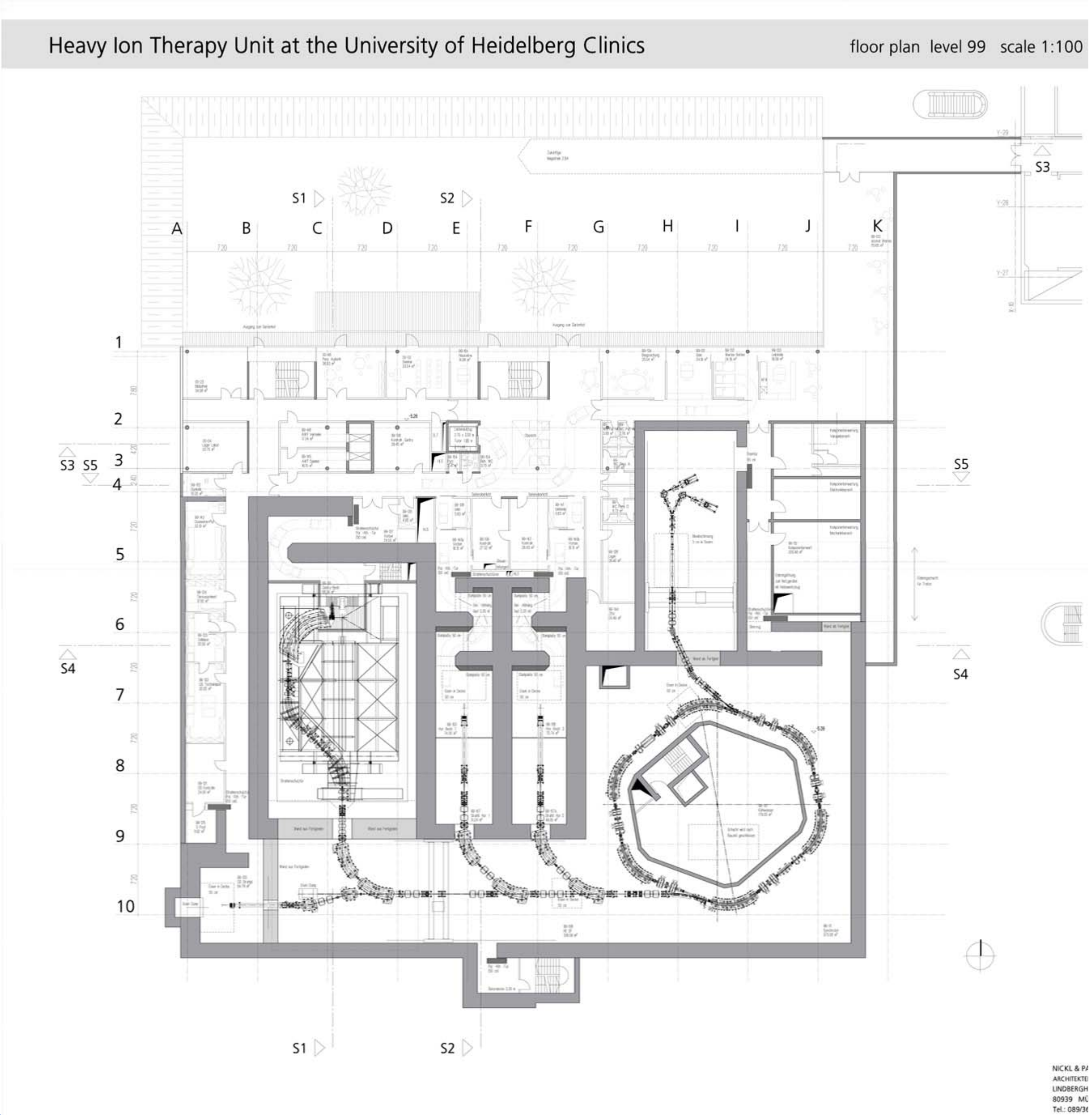
IMXT vs C-12 for skull base tumors



- Lower integral dose for C-12
- Steeper dose gradients for C-12
- Reduced number of fields
- Nearly complete sparing of OAR possible

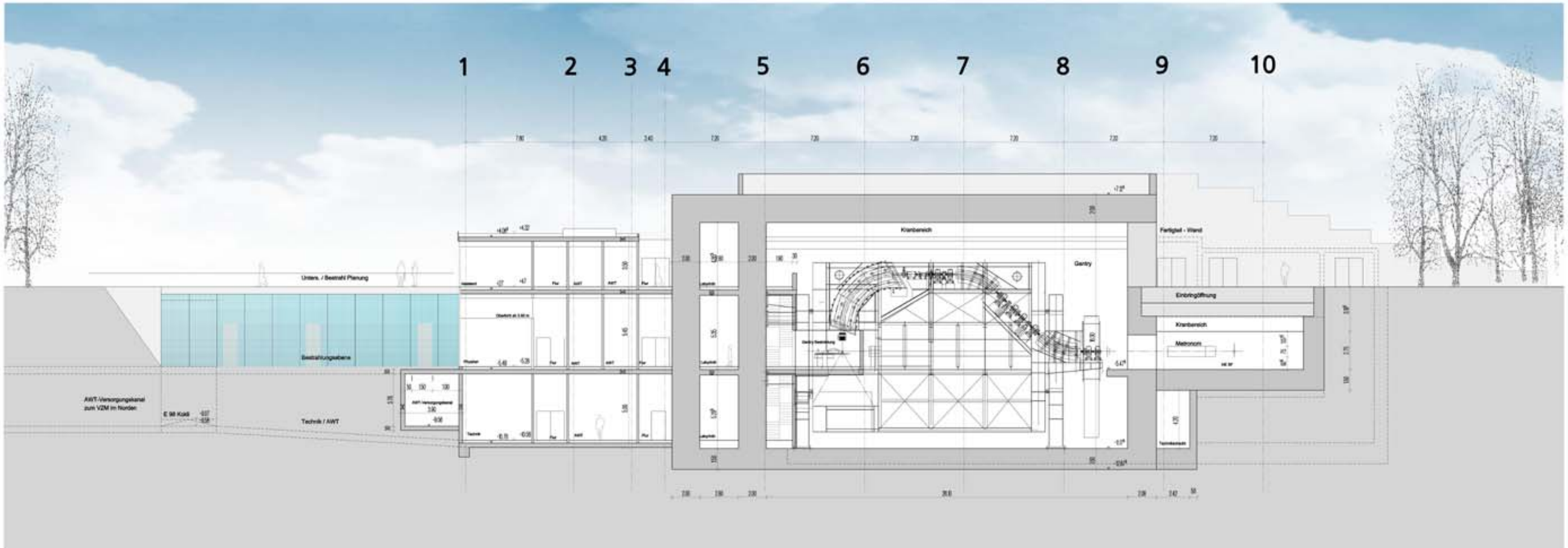
Outlook

- compact heavy ion synchrotron
- Isocentric gantry for ions
- p,He,C,O,... ions
- 1000 patients/yr
- In operation ~2006/2007



Heavy Ion Therapy Unit at the University of Heidelberg Clinics

Sections S1, S4   scale 1:100

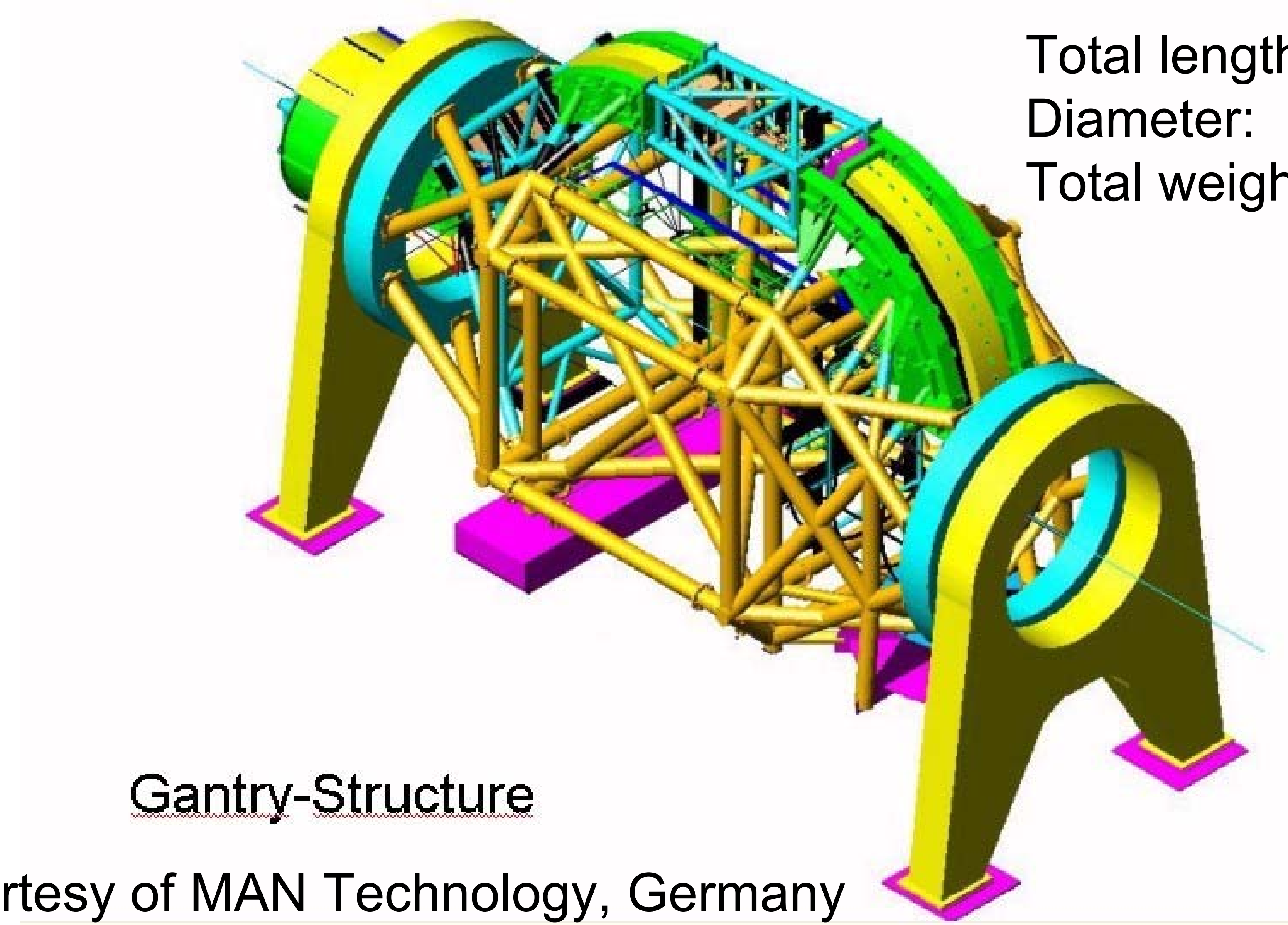


Section S1

Section S4

Model of the facility

Gantry concept



Total length: 20m
Diameter: 12m
Total weight: 600t

Courtesy of MAN Technology, Germany

Conclusion

Demonstration of feasibility + safety of scanned carbon ions in clinical routine for 230 patients

Outcome for Ch/CS of skull base comparable to protons for ACCa. as for neutrons, but only mild side effects

Good agreement of observed / predicted rate of side effects from radiobiological model

High future potential for heavy ions,

- if organ movement can be tracked online

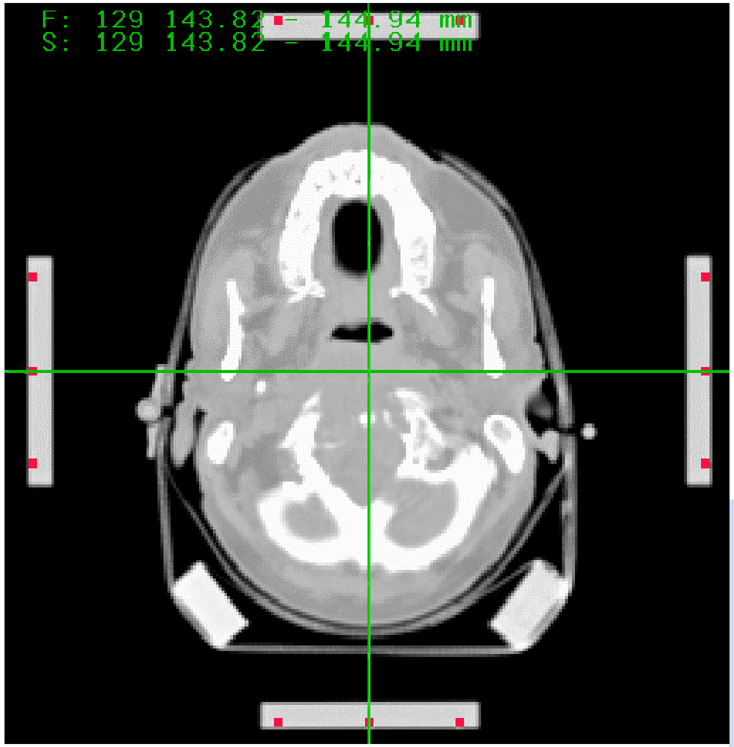
- if Intensity modulation is at the same level of IMXT

- if clinical studies show benefit for other tumors/ions

Thank you for your attention !

Stereotactic Imaging

“Fiducials” at stereotactic. ring visible in CT (Steel), MRI (Gd-DTPA), PET (Cu-64)



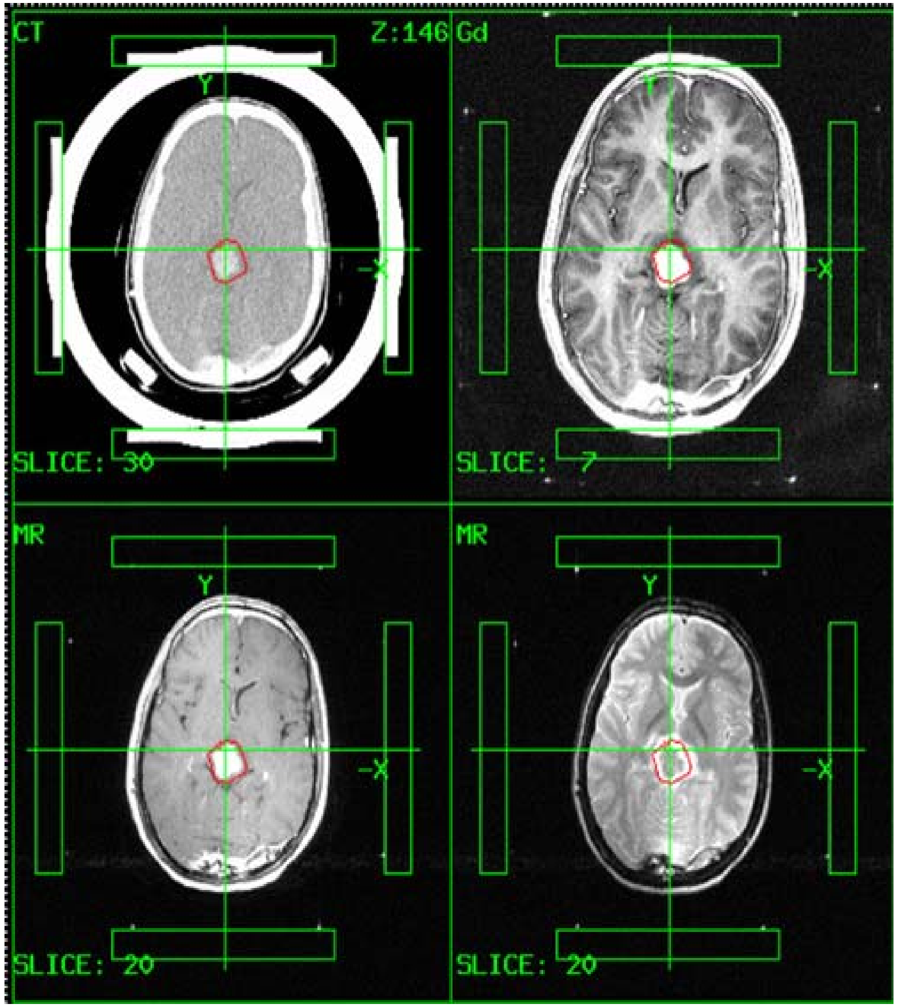
- Automated Detection
- Calculation of st. coordinates
- Correction of misaligned

Stereotactical Image correlation for target definition:

Brain metastasis

X-ray CT

MRI 3d Turbo FLASH Sequence with contrast



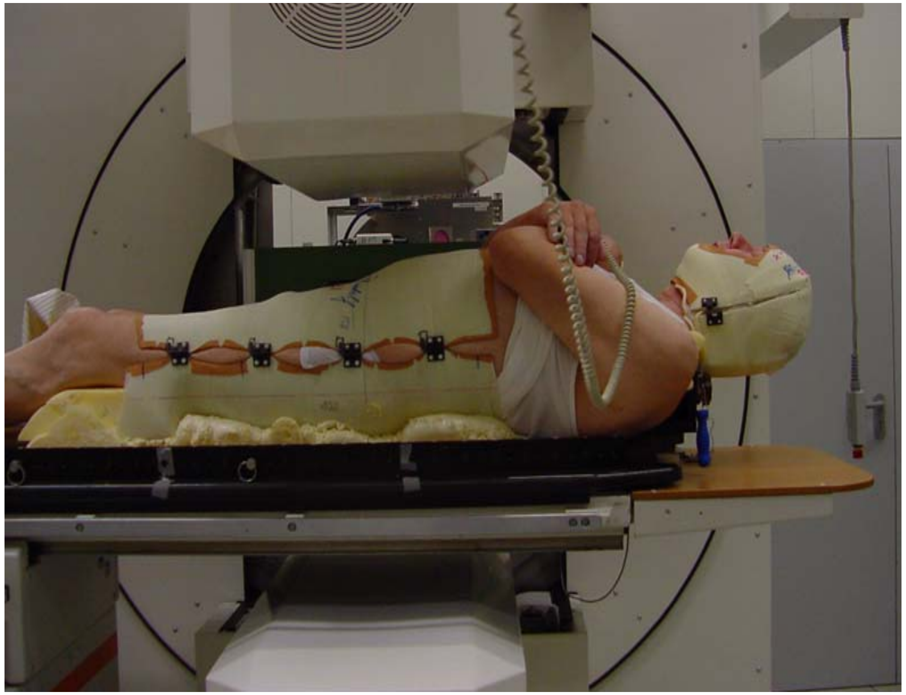
MRI Spin-Echo-Sequence

MRI T2 weighted Spin Echo seq.

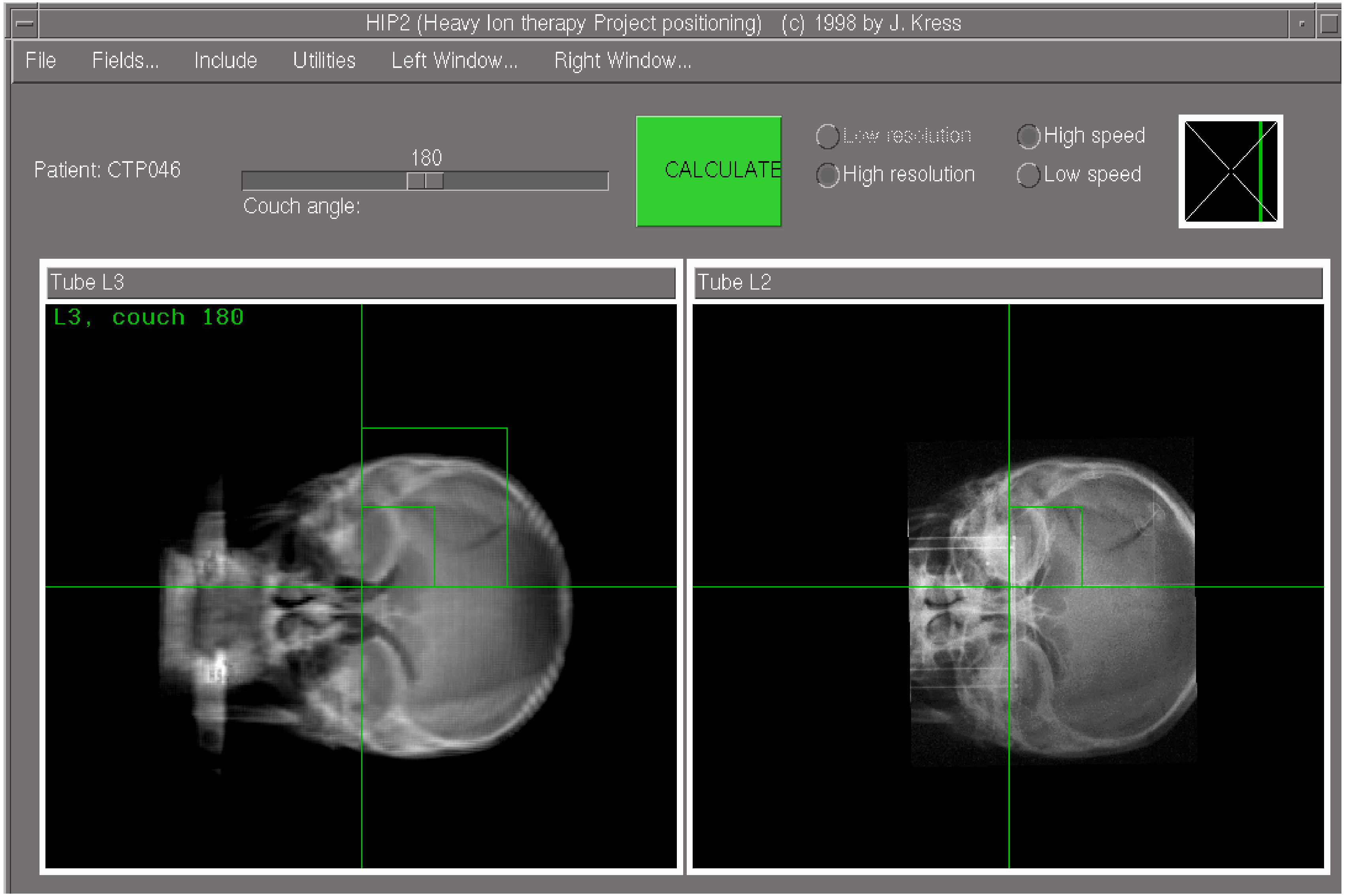
Patient Fixation and Stereotactic Positioning

Head mask and Stereotactic setup

Body frame fixation



Position control using X-rays and DRR



Accuracy for positioning around 1mm required !