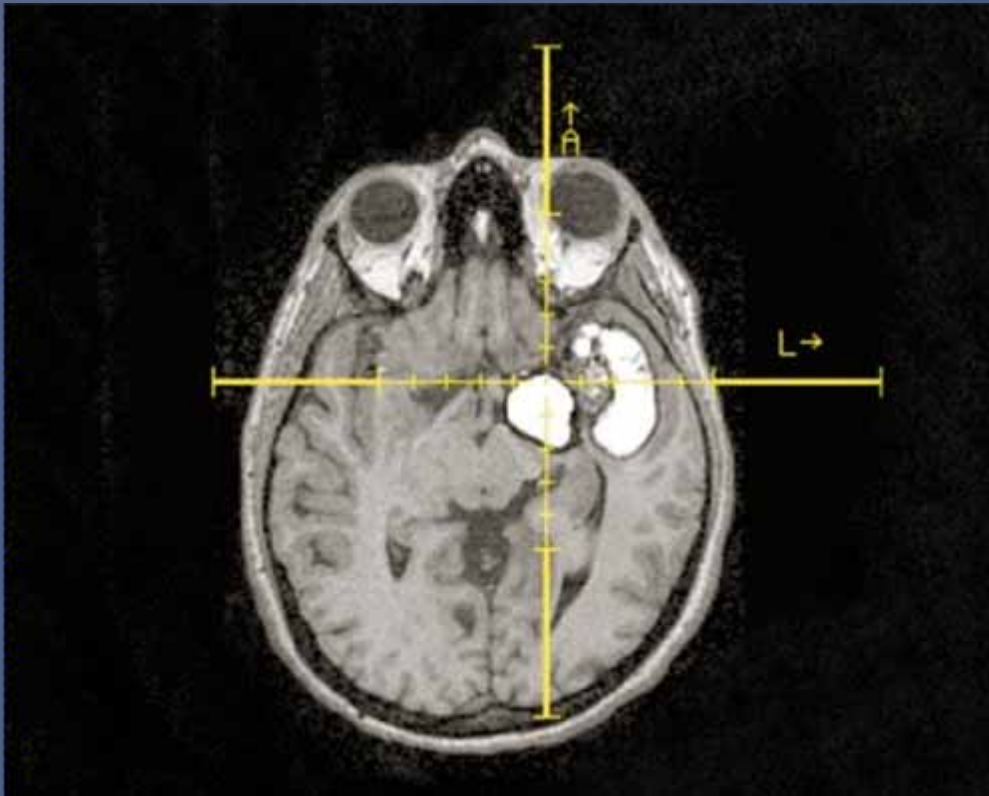


# Partikelterapi

Fysiklærer dag 2008, IFA, Århus

Niels Bassler  
Aarhus Universitetshospital og  
Deutsches Krebsforschungszentrum, Heidelberg



- Stråleterapi, i bedste fald:

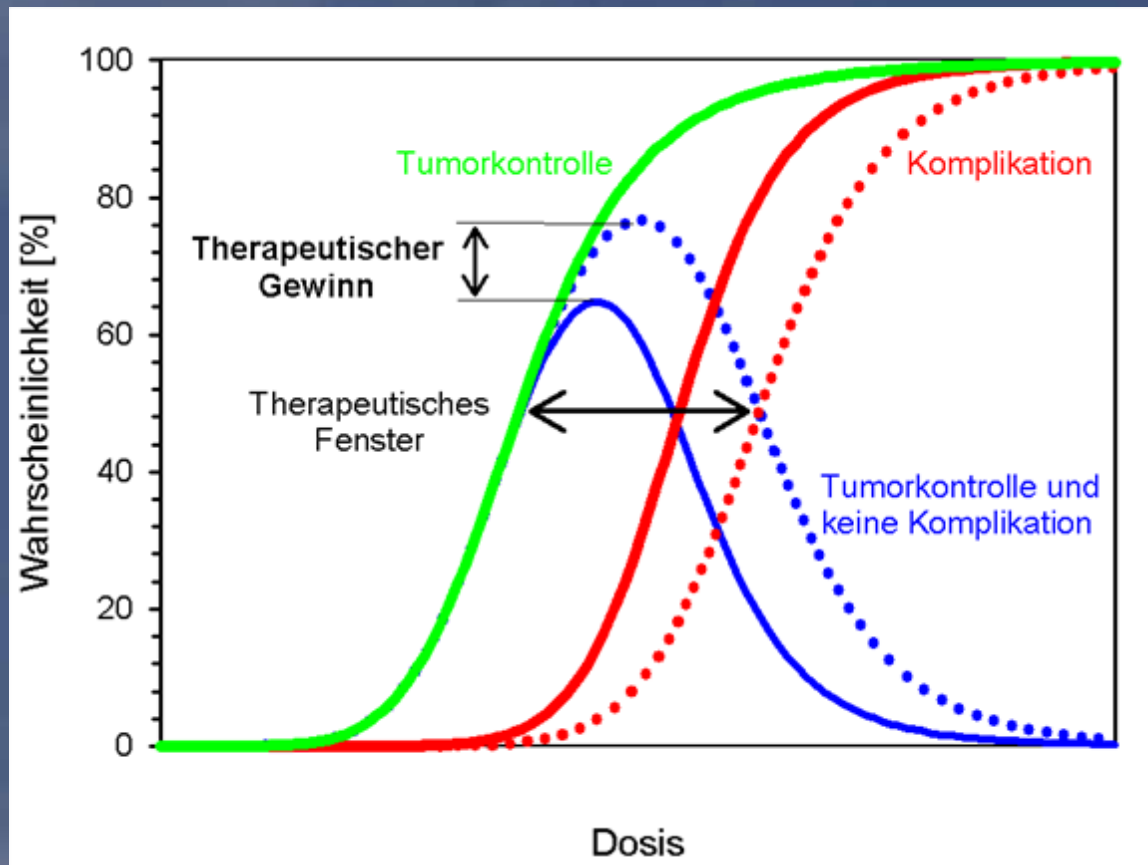
  - 100 % dosis i svulsten

  - 0 % dosis i det raske væv

- Dosis: afsat energi per masseenhed  
Gray (J/kg)

# Rationalet for konform stråleterapi

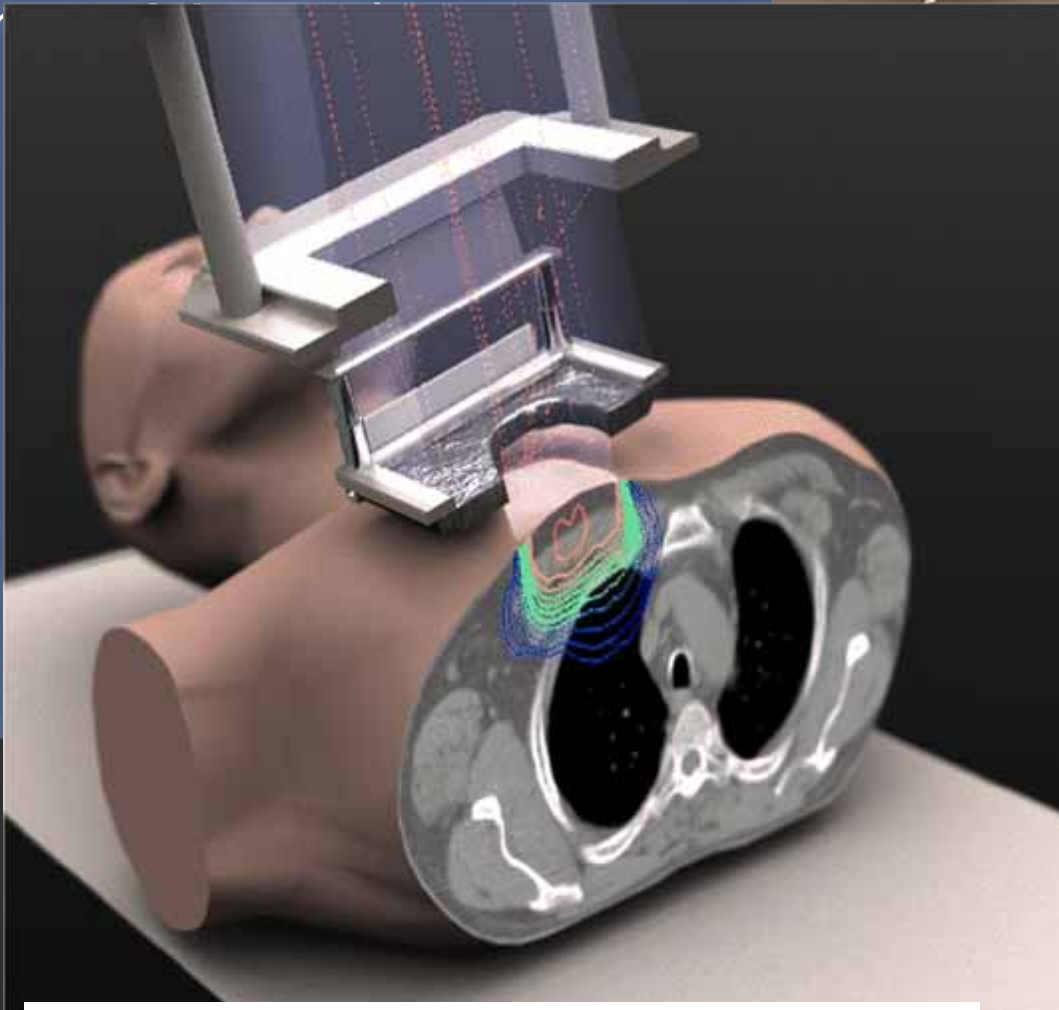
- Dosis (og tumorkontrol) i svulsten er begrænset af tolerancen af det raske væv / risikoorganerne (“organs at risk”).
- Volumeneffekt: jo mindre væv bestråles, jo højere tolerance af det raske væv.



Bedre konformitet af dosis muliggør højere dosis -> højere tumorkontrol uden at øge risiko for bivirkninger. (Obs: tumorkontrol ⊕ overlevelse)

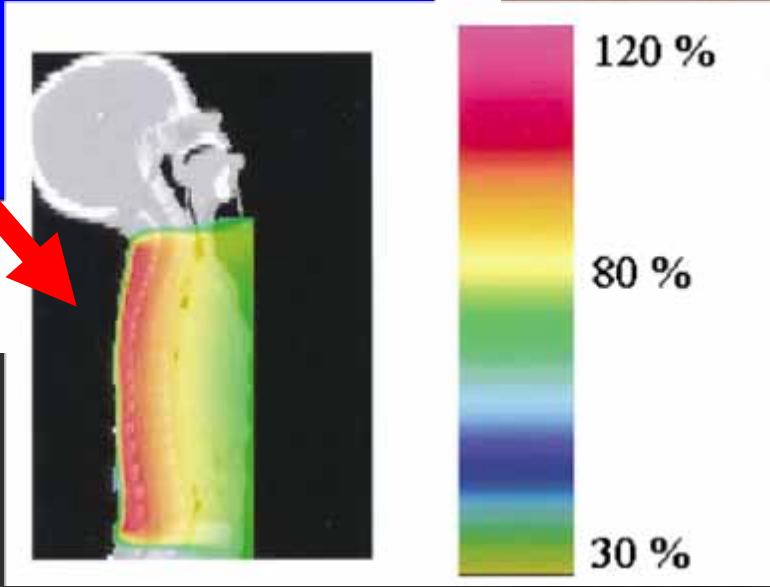
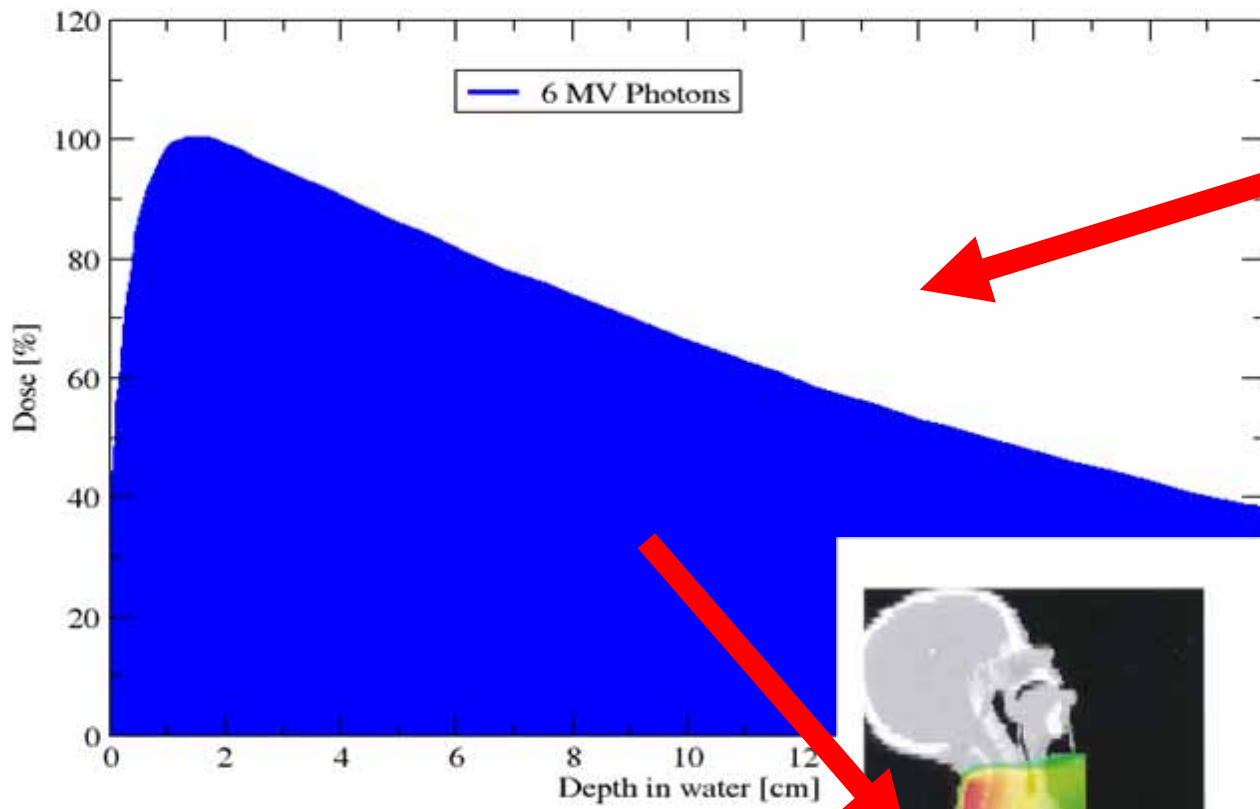
## ● Konventionel stråleterapi

(Røntgen)



(Rendering produced by Tomas Lundberg of MDS-Nordion.)





Clair et. al.



Lette partikler (elektroner, fotoner) spreder meget ved passage gennem stof => ringe konformitet.

Tungere partikler spreder mindre, stråleterapi med partikler?

**Protoner (siden 60erne)**

**56000 patienter behandlet.  
25 aktive centre i dag.**

*(kilde: PTCOG, Jan 2008)*

**Ioner (He, Li, B... C, Ne..)  
(siden 1994)**

**3500 patienter behandlet i 3  
centre.**

**Antiprotoner**

**NYT!**

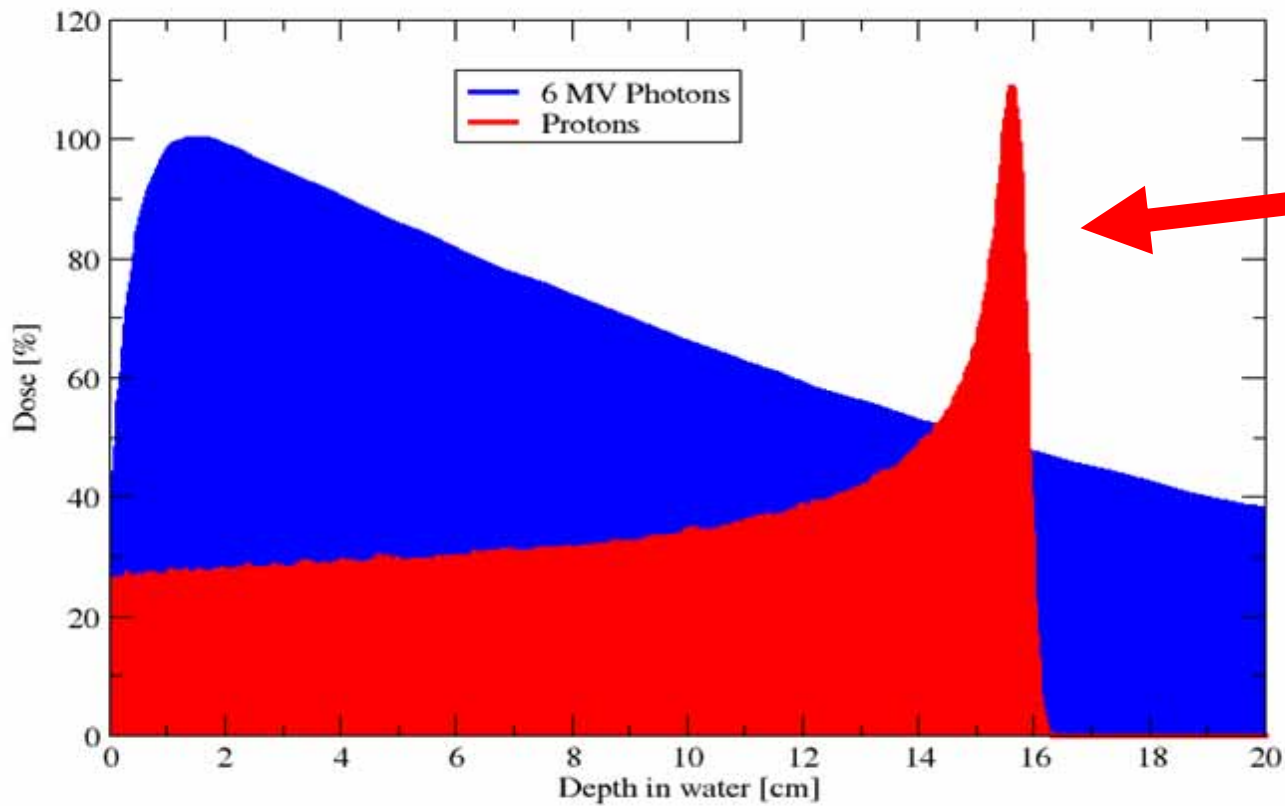
**0 patienter, 0 centre.**

(Stråleterapi med neutroner og pi-mesoner, blev også anvendt på patienter.)

# Protonterapi



# Protonterapi

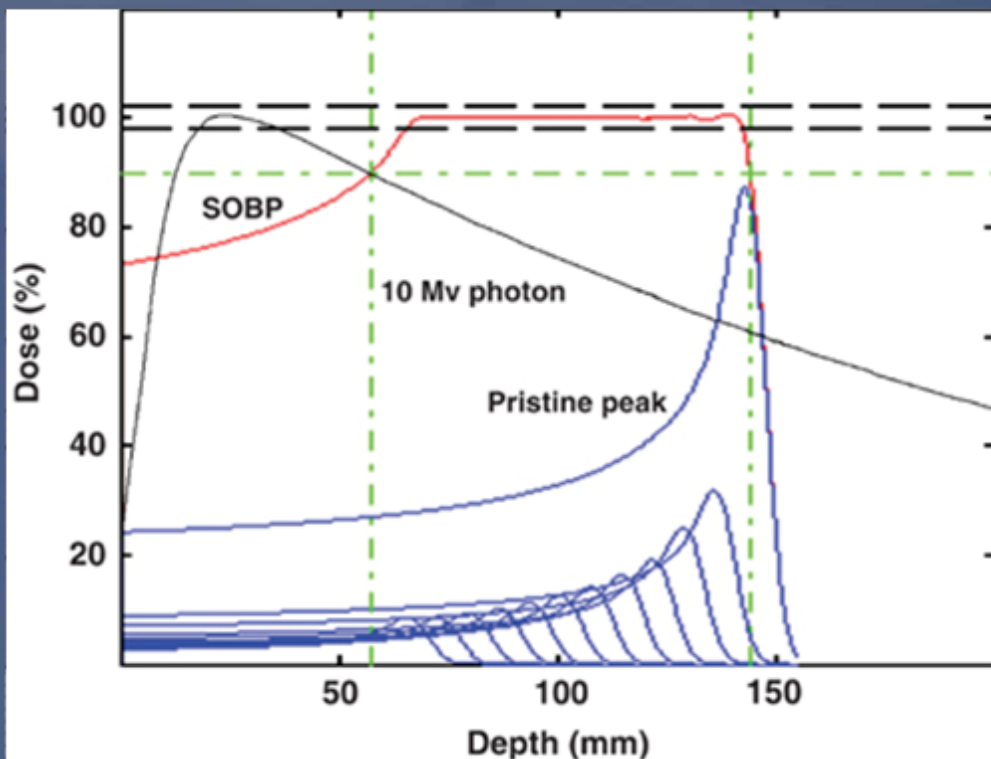


150 MeV Protoner

Bragg-peak

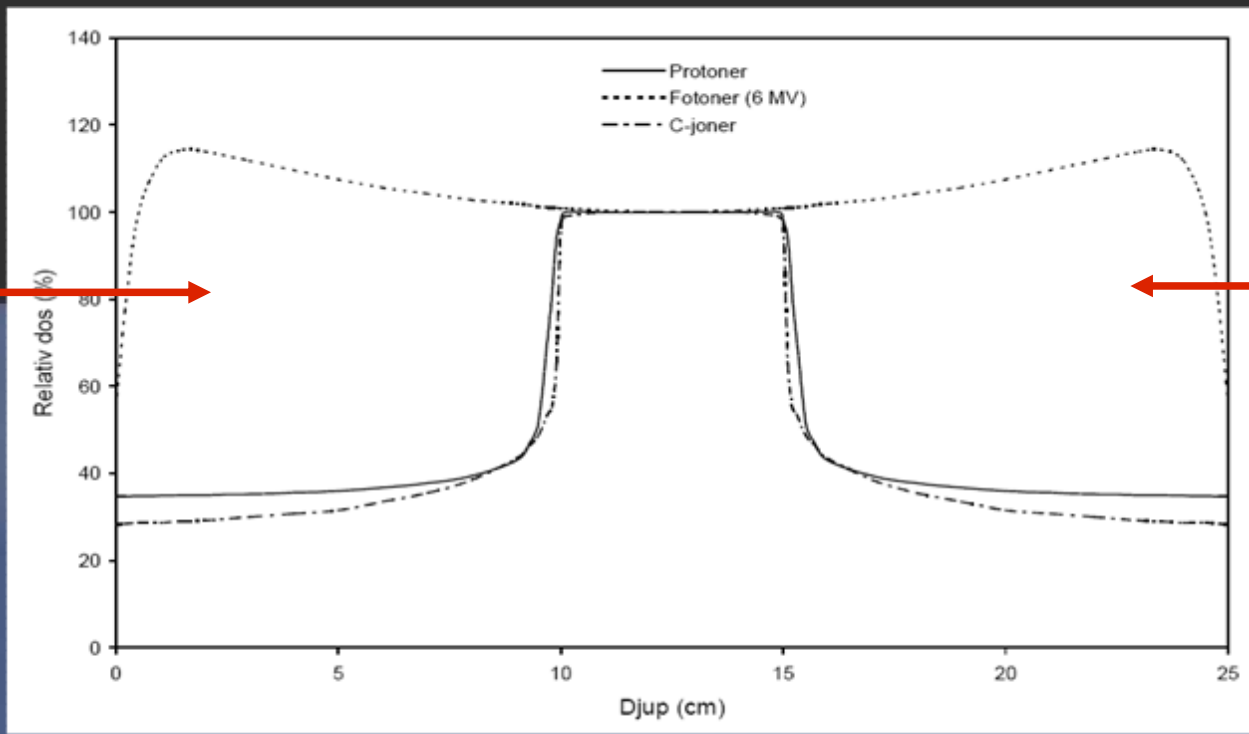


# ”Spread out Bragg Peak”

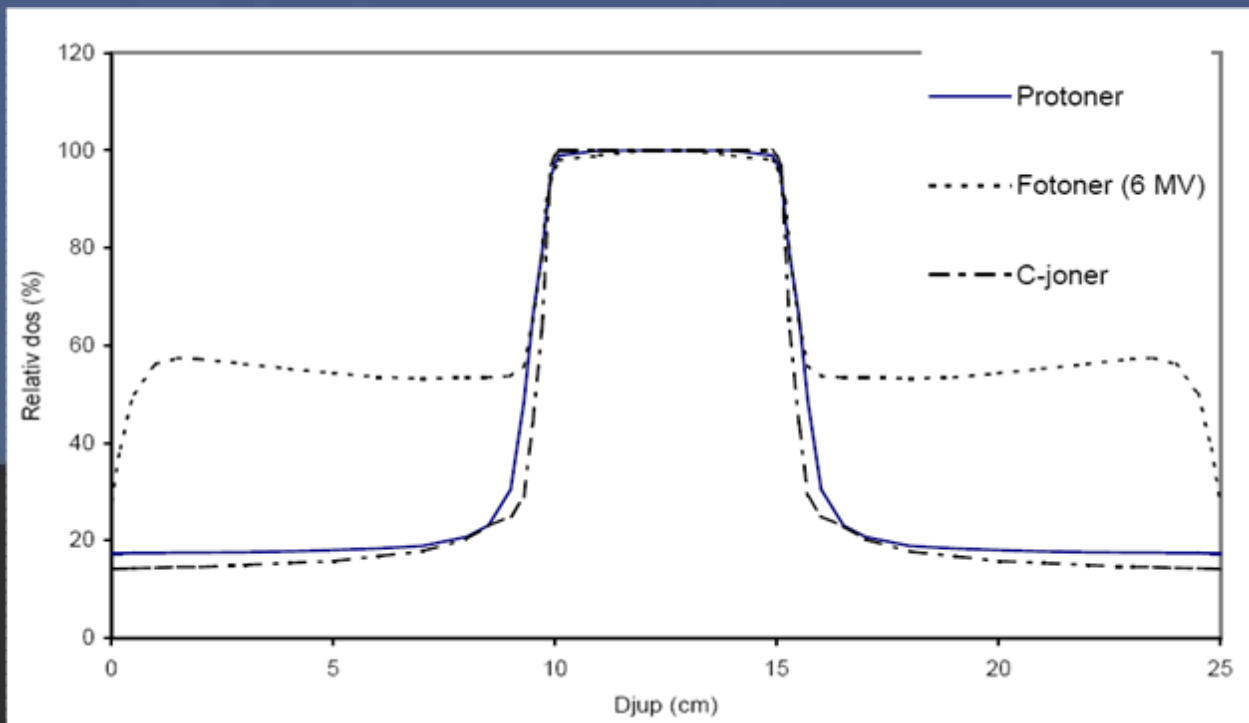


SOBP =  
”Spread out Bragg Peak”

(psi.ch)



To opponerende  
 felter



fire felter

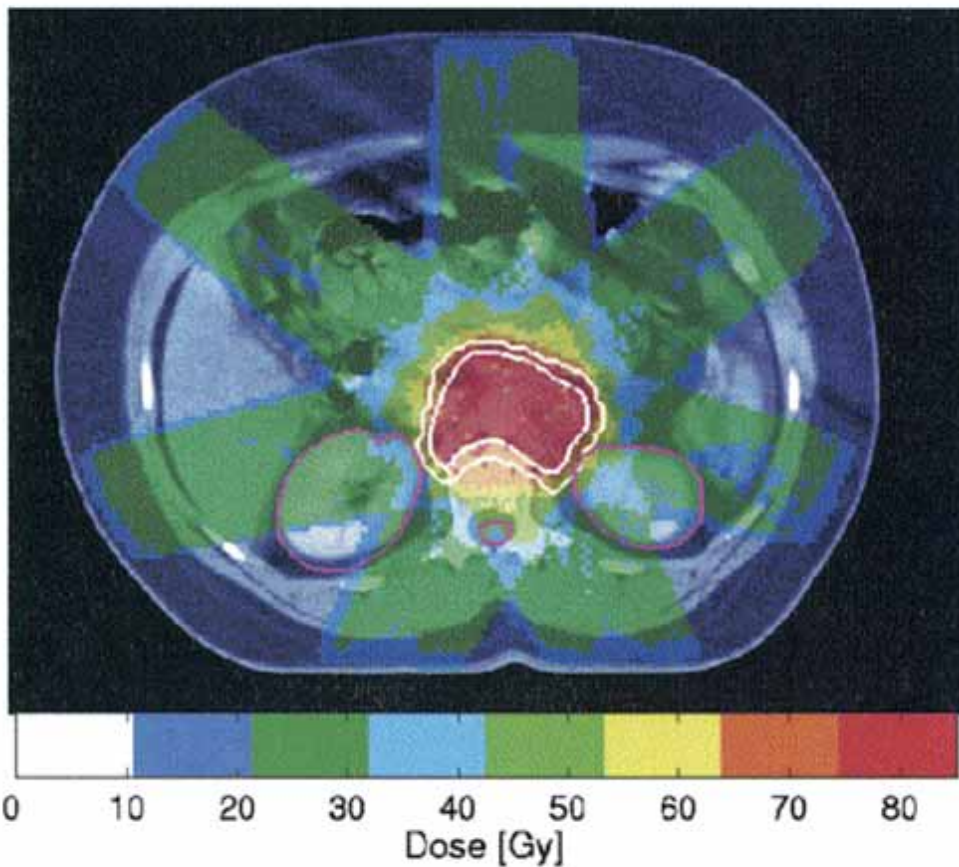
(SPTC, "Val av utrustning för strålbehandling med protoner, slutrapport 2003-010-05)

# Protonterapi vs. IMRT (Fotoner)

IMRT Fotoner

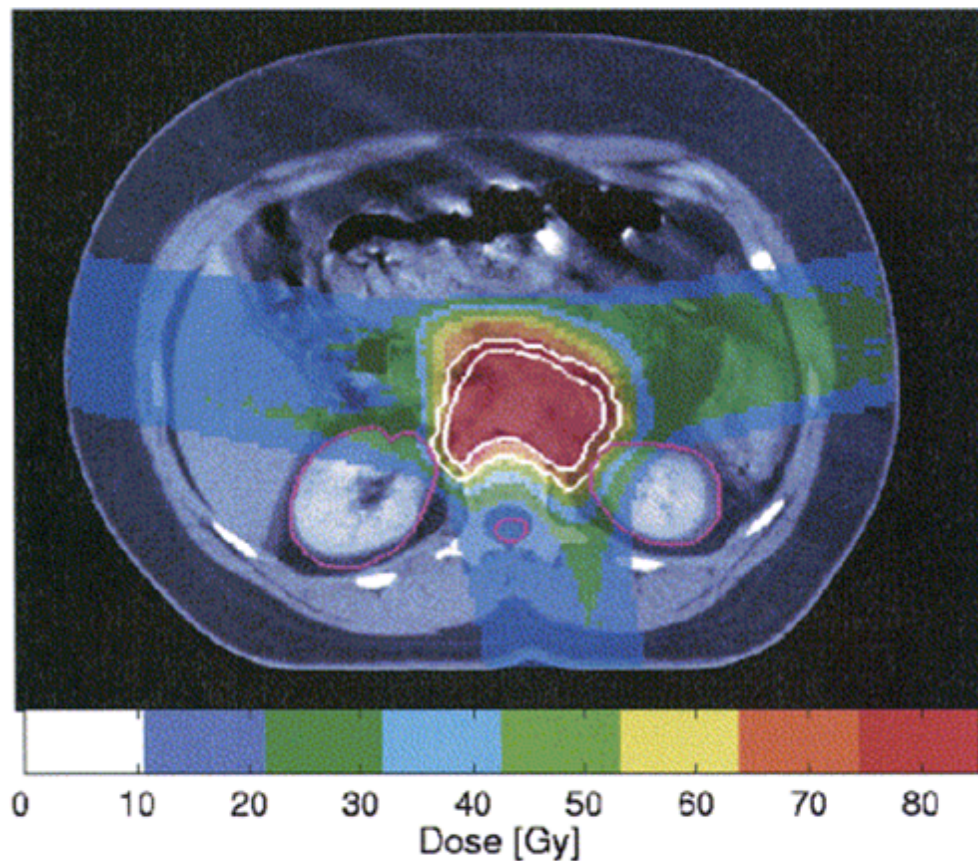
IMPT Protoner

B:IMRT



(c)

B:IMPT



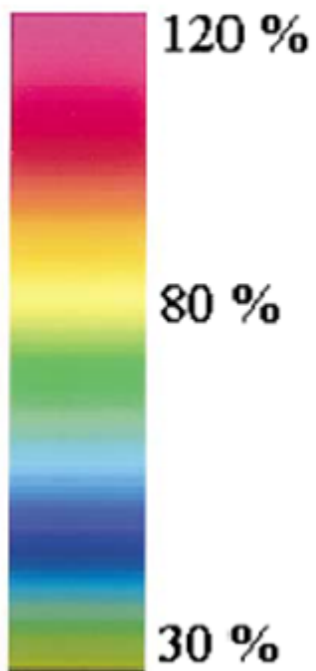
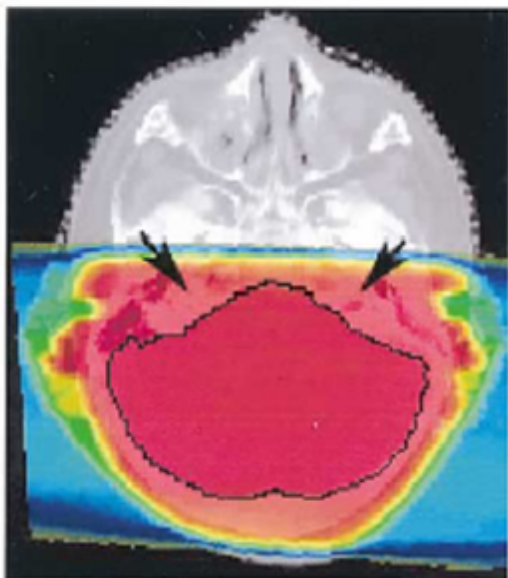
(d)

Weber et. al.

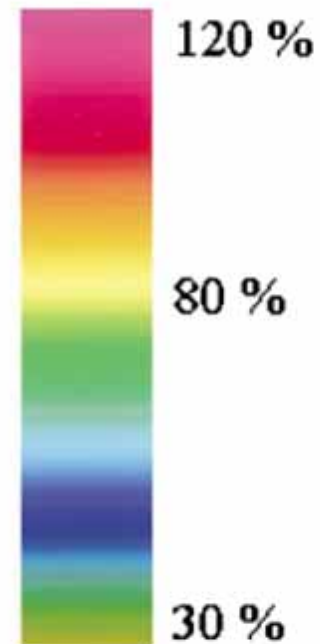
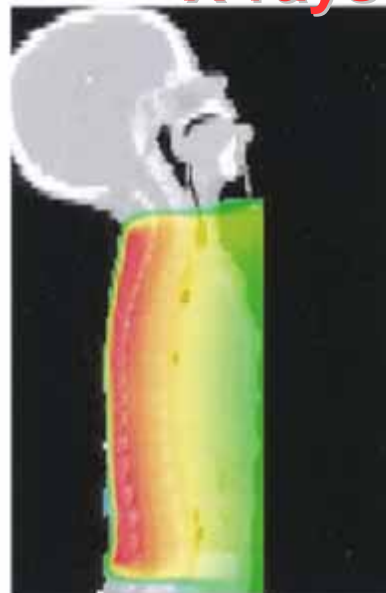


# Protonterapi (Medulloblastoma)

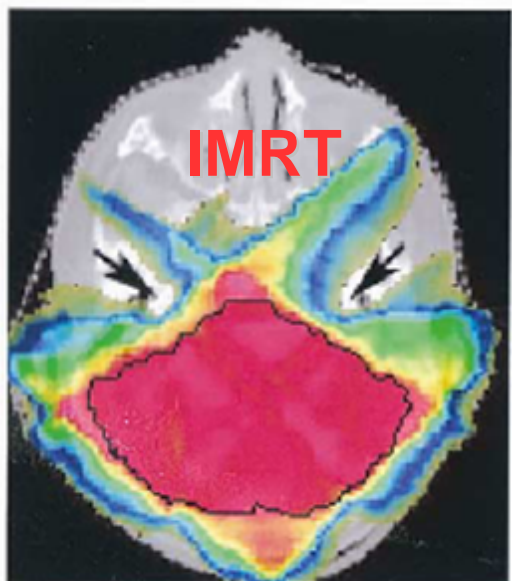
**X-rays**



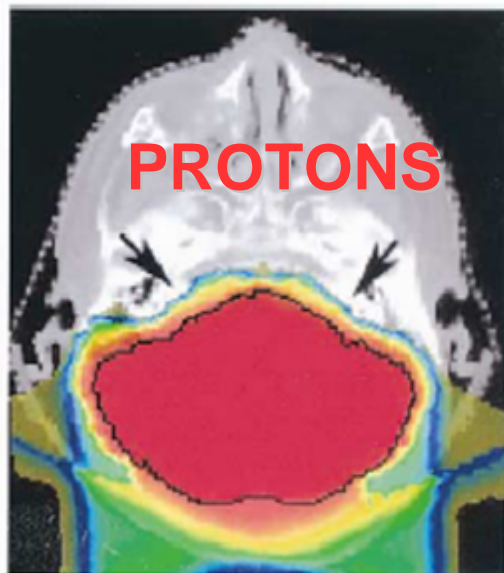
**X-rays**



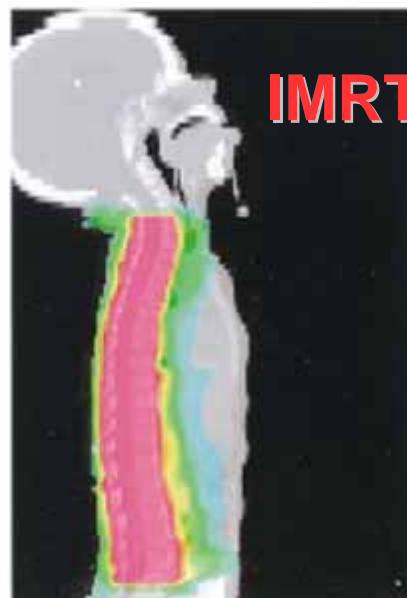
**IMRT**



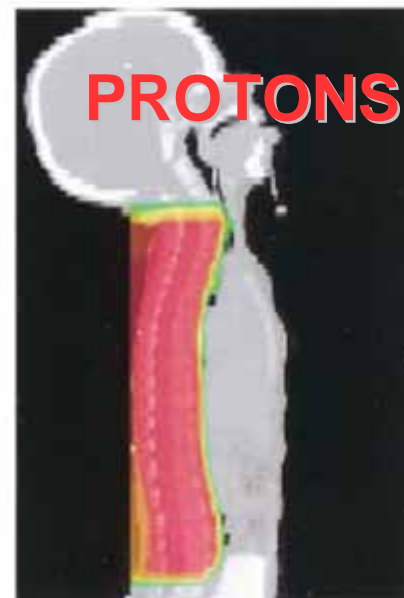
**PROTONS**



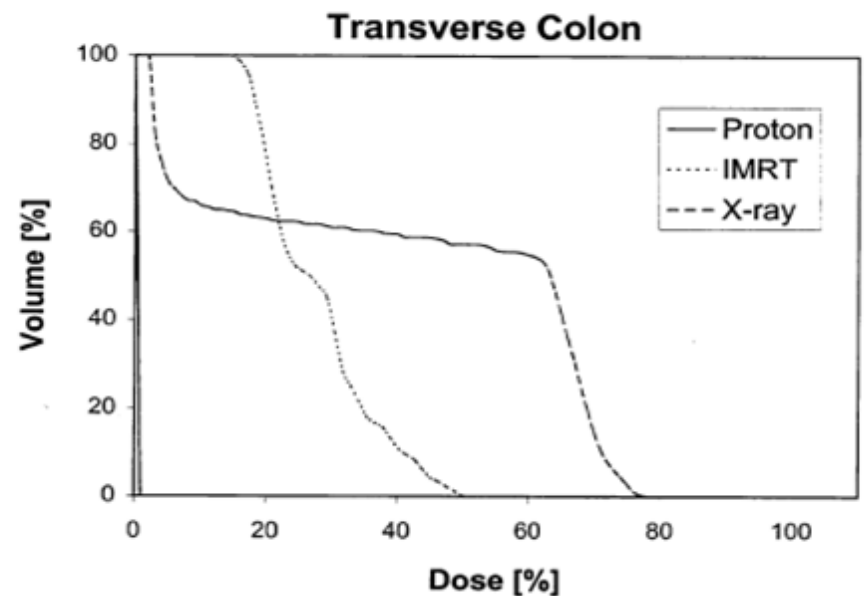
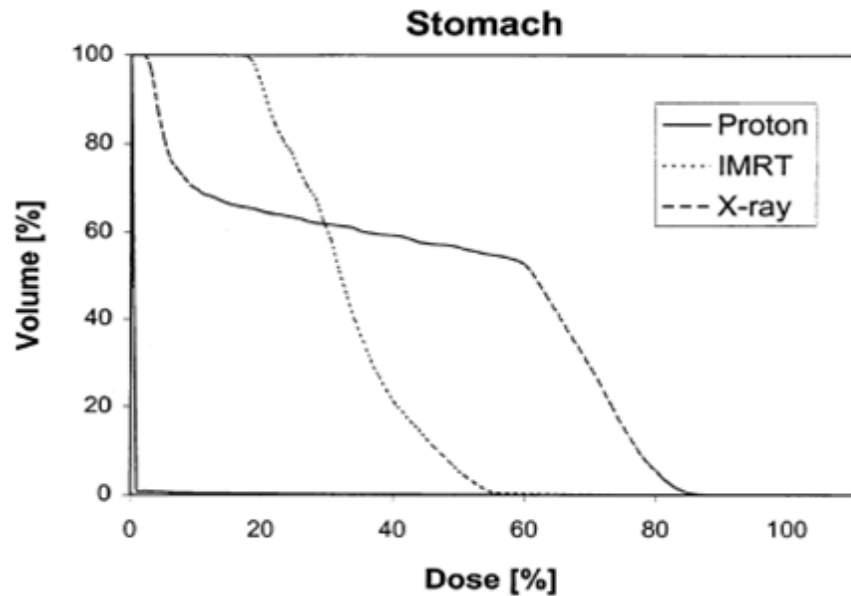
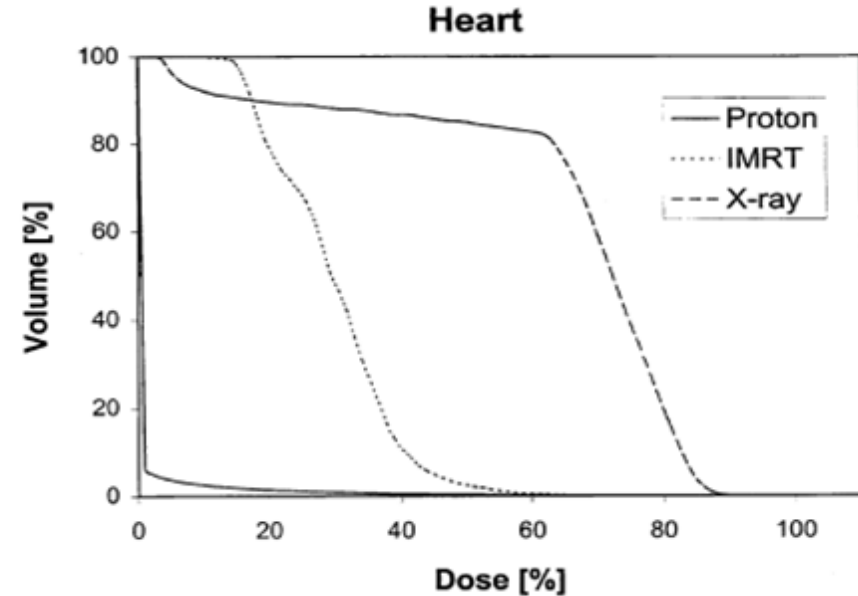
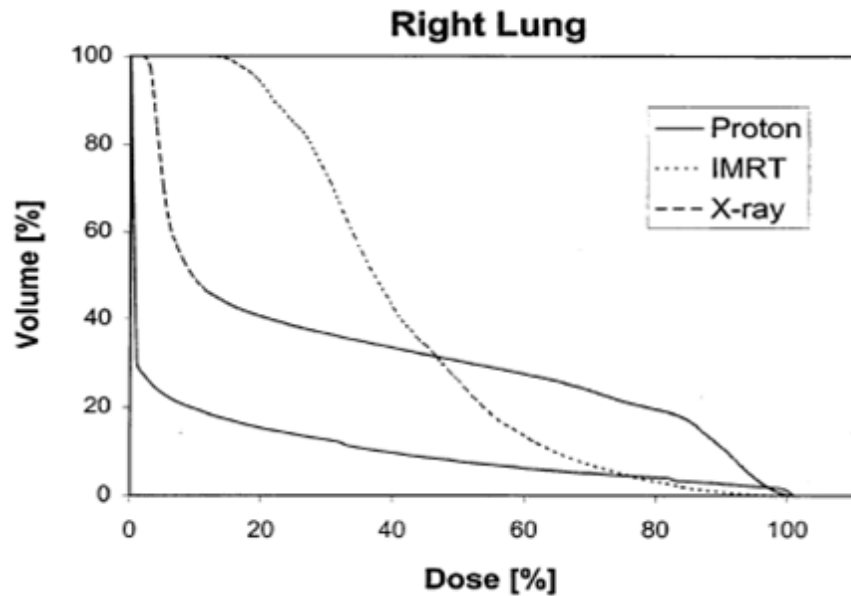
**IMRT**



**PROTONS**



# Protonterapi (Medulloblastoma)



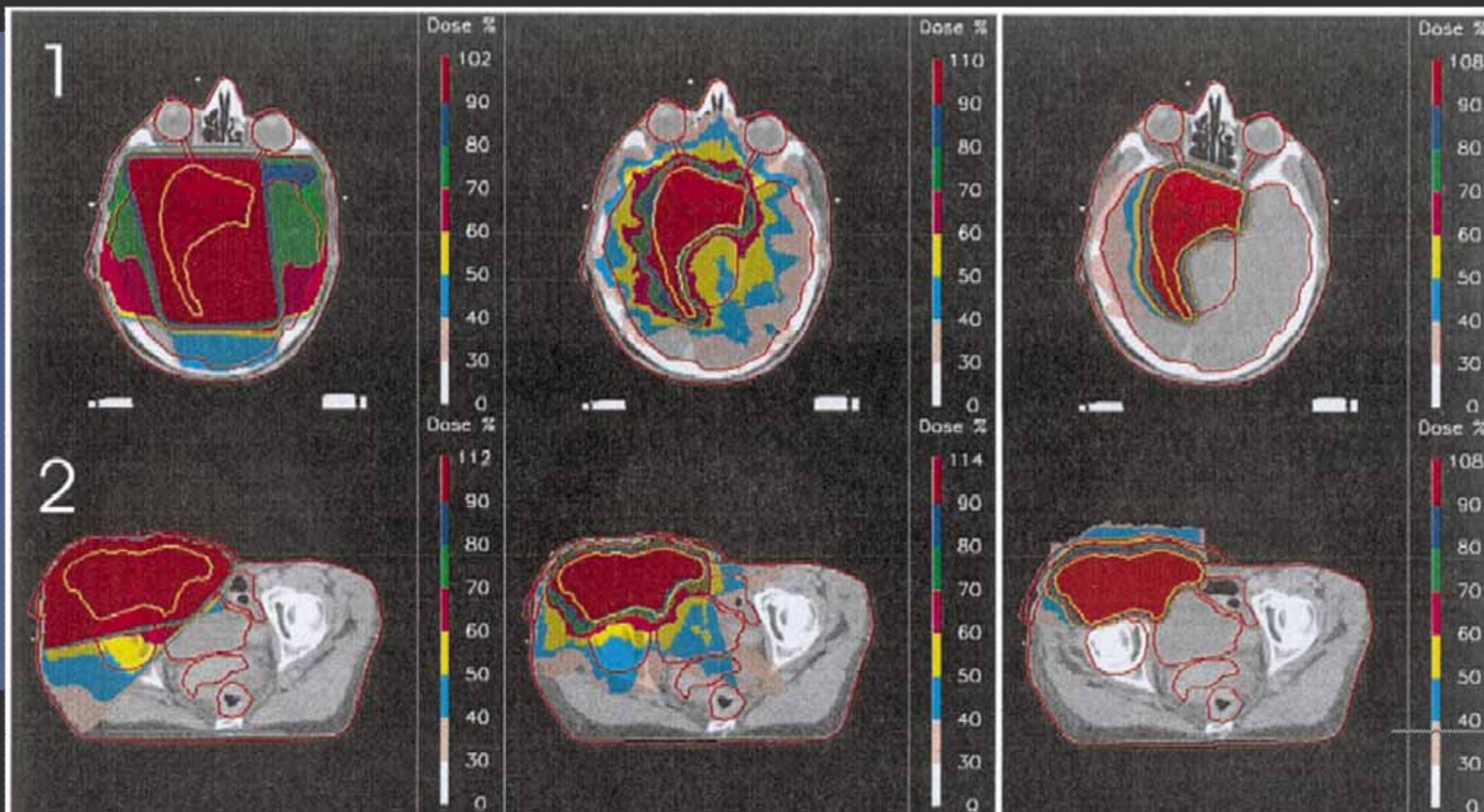


# Protonterapi

Photons

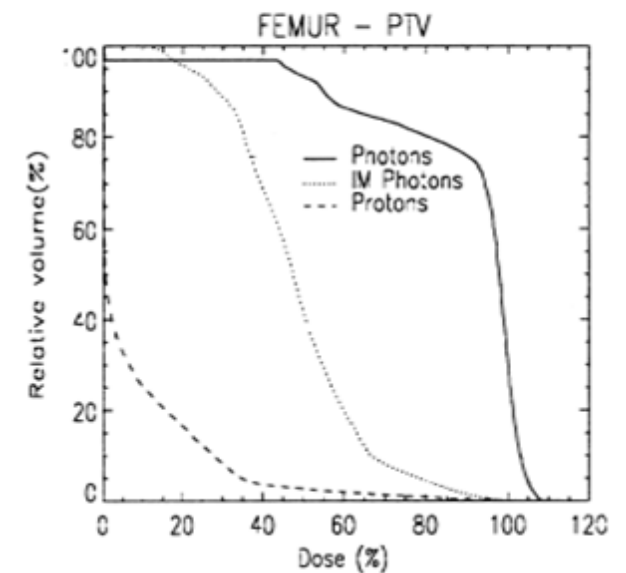
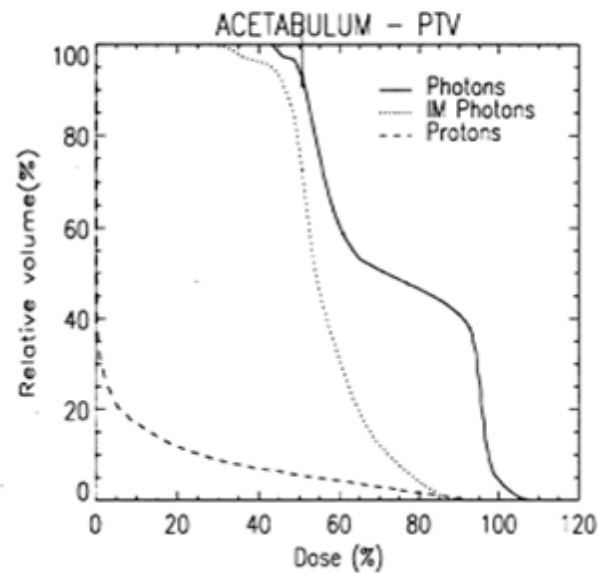
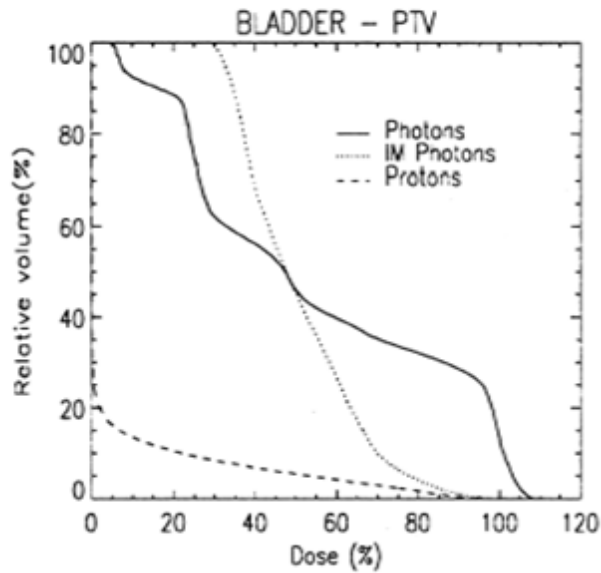
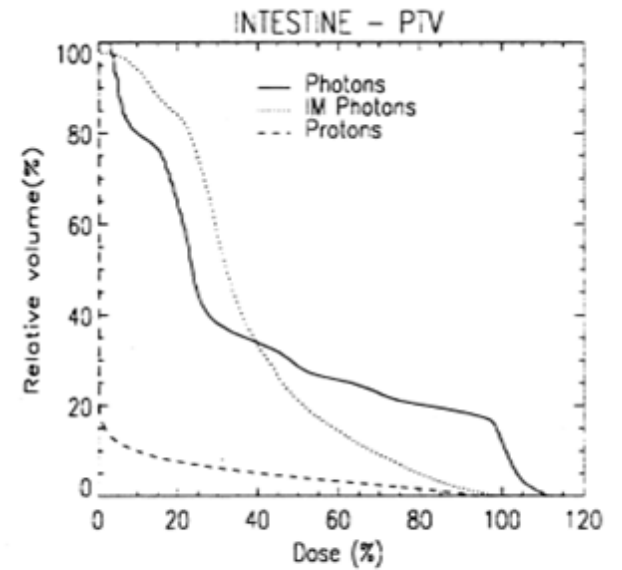
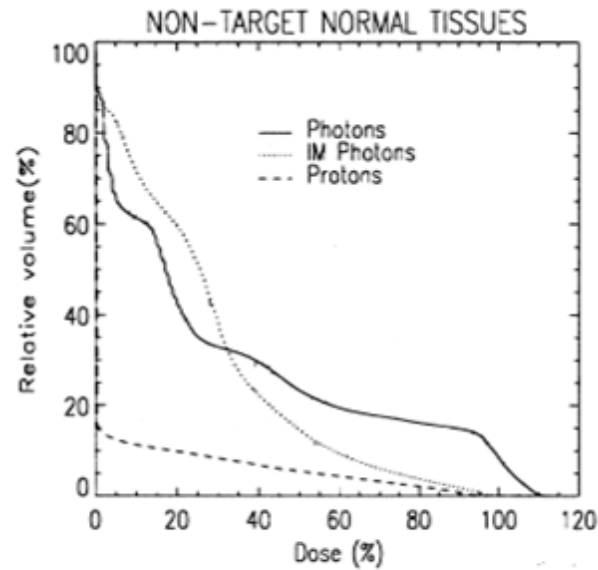
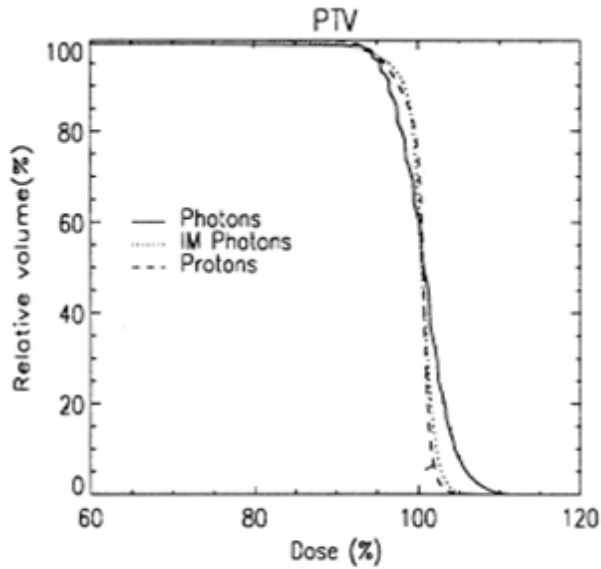
IMRT

Protons



Lomax et. al.

2) Malignant melanoma





# Teknik



(Fermilab)

### Loma Lindas Proton Synkrotron bygget af Fermilab, USA

- \* ~ 8 m diameter
- \* pulset
- \* energiskift fra puls til puls (varierer indtrængningsdybde)



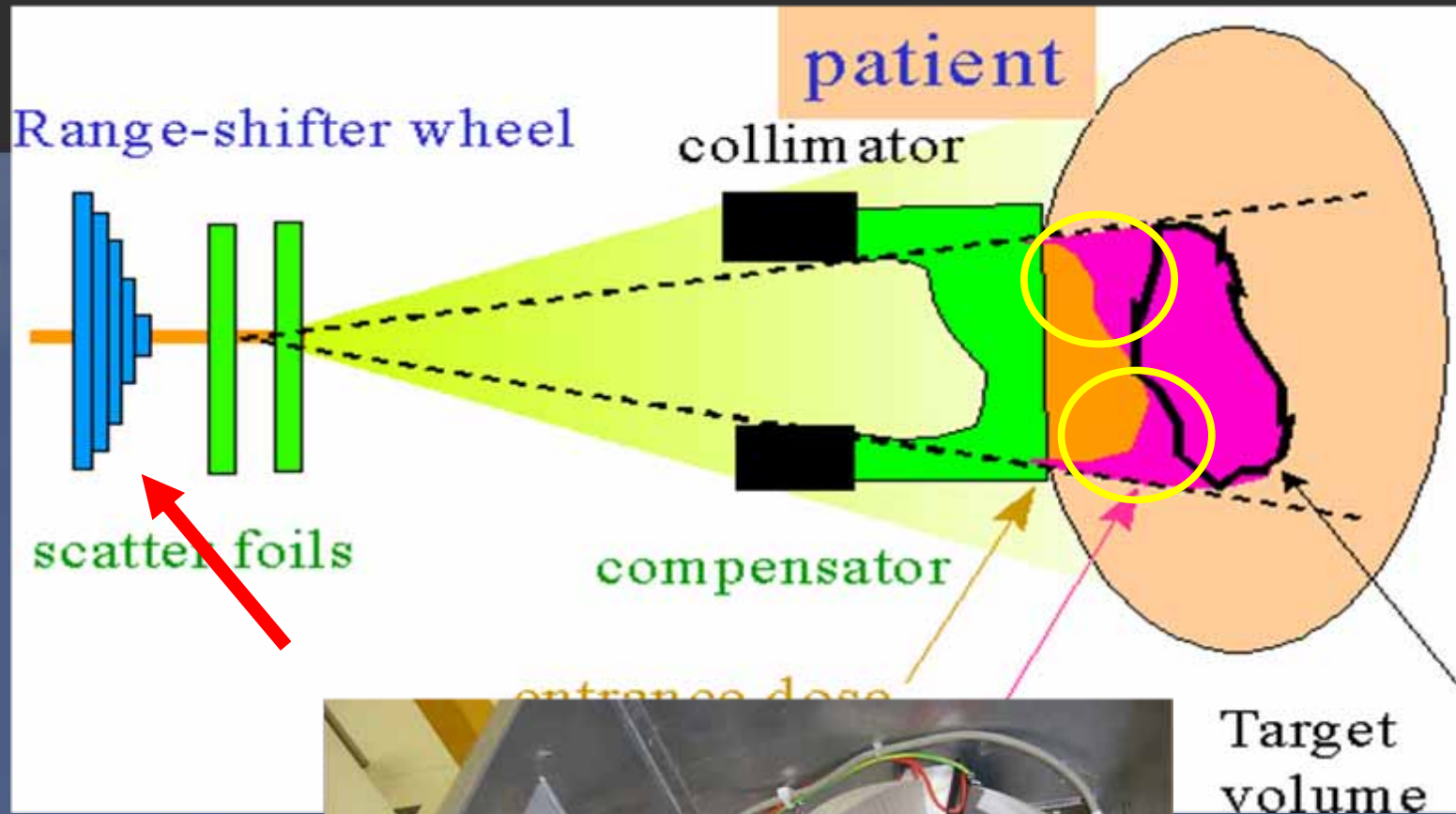
### Superledende Proton Cyklotron for Protonterapi, bygget af ACCEL (Tyskland)

(ACCEL)

- \* ~ 3 m diameter
- \* DC, høj strøm (500nA)
- \* nem at vedligeholde

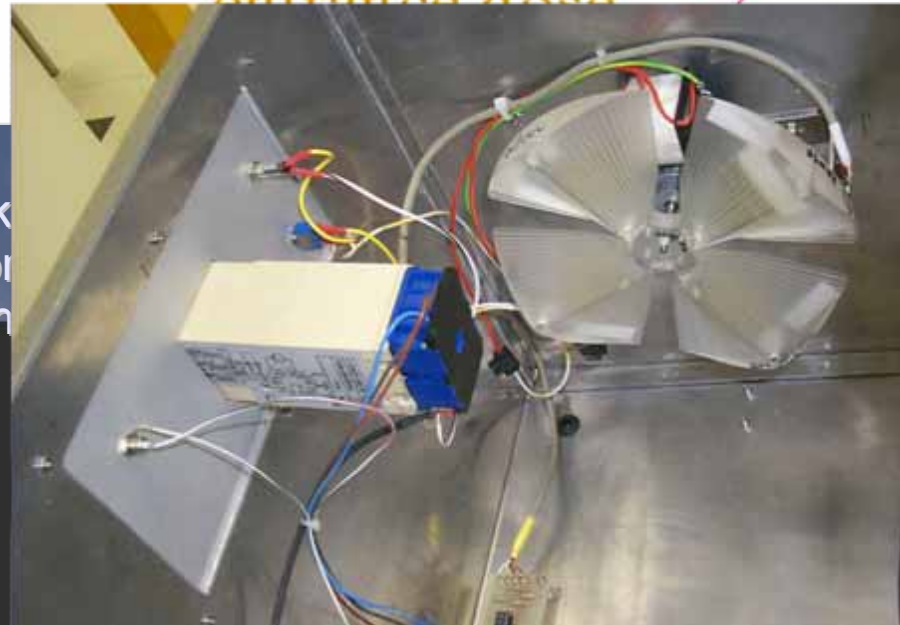
\* fast energi, -> indtrængningsdybden varieres ved at putte materiale ind i beamet (Degradere)

# Passiv spredning af beam



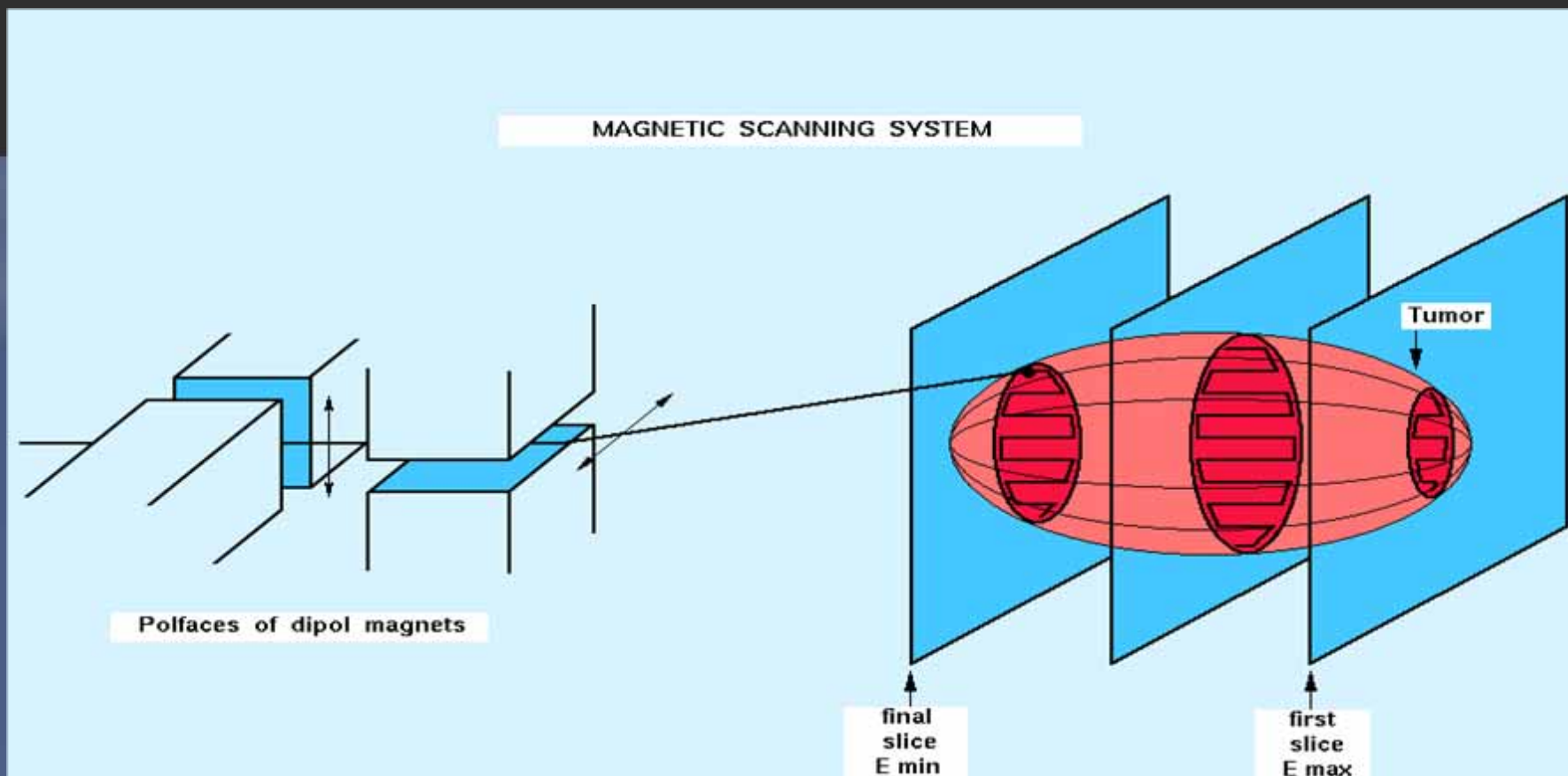
(psi.ch)

- "gammel" teknik
- brugt ved fx. LOR
- cyklotroner er mere præcise langs z-aksen.



brugt til at sprede beamet ud

# Spot scanning ("Raster scanning")

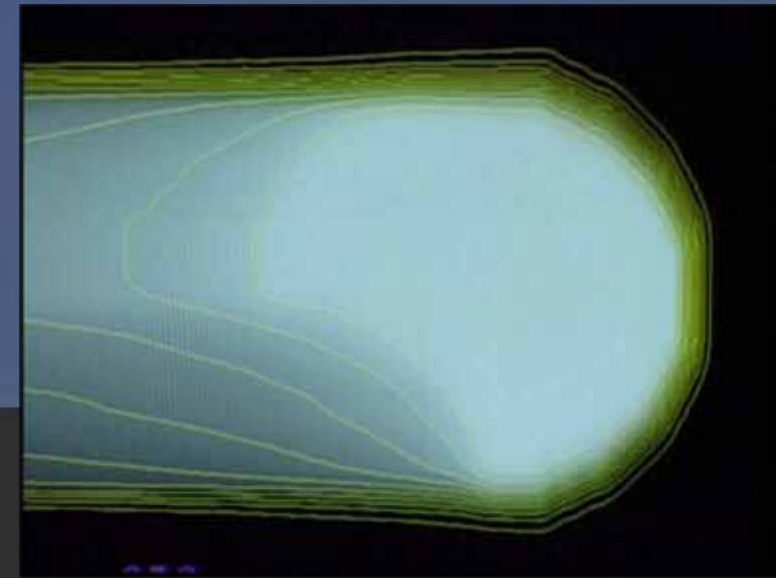
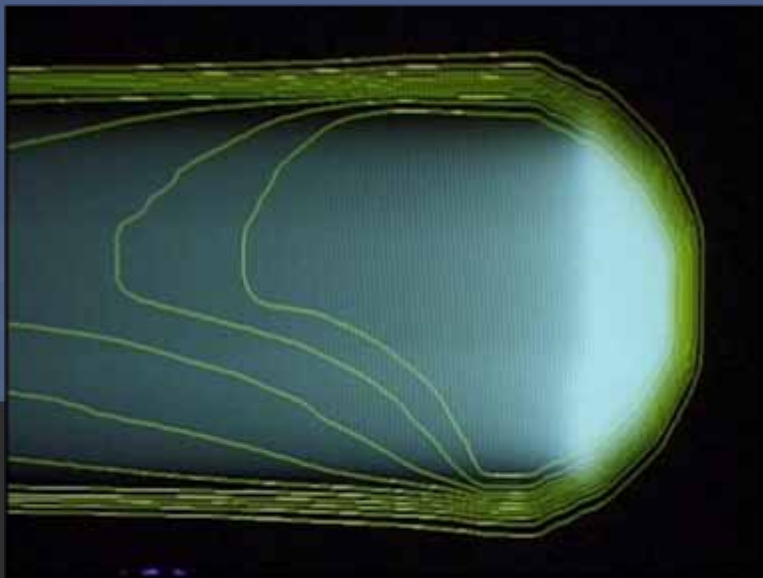
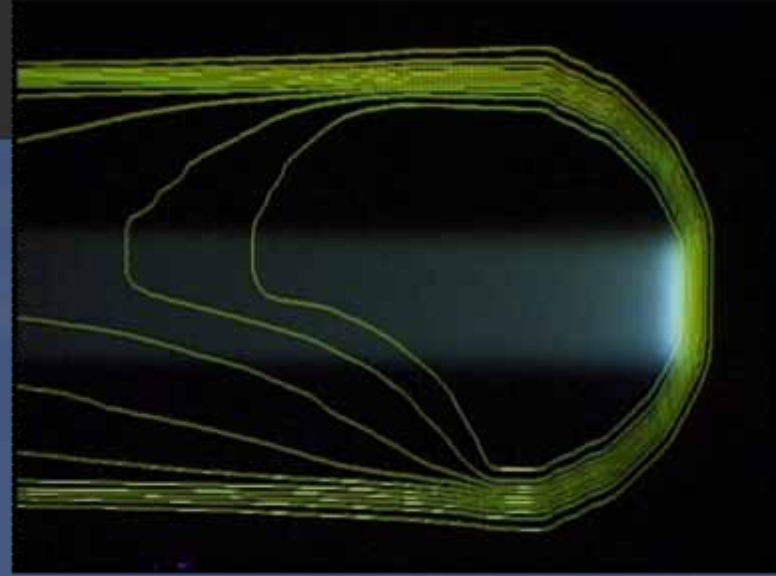
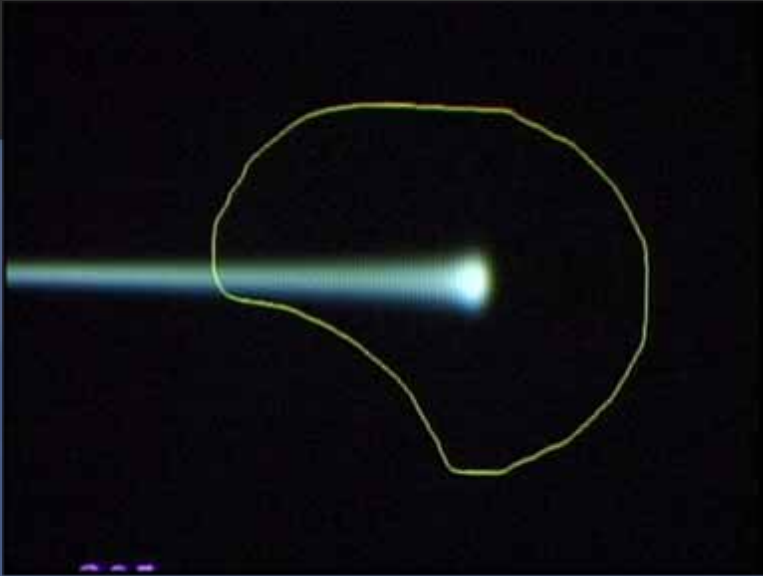


(gsi.de)

- ny teknik, udviklet og brugt ved PSI, GSI
- dybde-modulation enten via synkrotron eller en degrader for cyklotron



# Spot scanning ("Raster scanning")



Spot scanning at PSI

# Aktive faciliteter for partikelterapi

(Jan 2008)

## Particle therapy facilities in operation:

WHO, WHERE	COUNTRY	PARTICLE	MAX. CLINICAL ENERGY (MeV)	BEAM DIRECTION	START OF TREATMENT	TOTAL PATIENTS TREATED	DATE OF TOTAL
ITEP, Moscow	Russia	p	250	horiz.	1969	4024	Dec-07
St.Petersburg	Russia	p	1000	horiz.	1975	1327	Dec-07
PSI, Villigen	Switzerland	p	72	horiz.	1984	4875	Dec-07
Dubna	Russia	p	200***	horiz.	1999	402	Dec-07
Uppsala	Sweden	p	200	horiz.	1989	738	Dec-06
Clatterbridge	England	p	62	horiz.	1989	1701	Dec-07
Loma Linda	CA.,USA	p	250	gantry,horiz.	1990	11414	Nov-06
Nice	France	p	65	horiz.	1991	3129	Sep-06
Orsay	France	p	200	horiz.	1991	3766	Dec-06
iThemba Labs	South Africa	p	200	horiz.	1993	500	Dec-07
MPRI(2)	IN.,USA	p	200	horiz.	1993	220	Sep-06
UCSF	CA.,USA	p	60	horiz.	1994	920	Mar-07
HIMAC, Chiba	Japan	ion	800/u	horiz.,vertical	1994	2867	Aug-06
TRIUMF, Vancouver	Canada	p	72	horiz.	1995	130	Dec-07
PSI, Villigen	Switzerland	p**	250*	gantry	1996	320	Dec-07
G.S.I. Darmstadt	Germany	ion**	430/u	horiz.	1997	316	July-06
HMI, Berlin	Germany	p	72	horiz.	1998	1014	Dec-07
NCC, Kashiwa	Japan	p	235	gantry	1998	462	Nov-06
HIBMC,Hyogo	Japan	p	230	gantry	2001	1658	Dec-07
HIBMC,Hyogo	Japan	ion	320	horiz.,vertical	2002	271	Dec-07
PMRC(2), Tsukuba	Japan	p	250	gantry	2001	1188	Dec-07
NPTC, MGH Boston	USA	p	235	gantry,horiz.	2001	2710	Oct-07
INFN-LNS, Catania	Italy	p	60	horiz.	2002	151	Dec-07
Shizuoka	Japan	p	235	gantry, horiz.	2003	410	Nov-06
Wakasa WERC,Tsuruga	Japan	p	200	horiz.,vertical	2002	33	Aug-06
WPTC, Zibo	China	p	230	gantry, horiz.	2004	537	Dec-07
MD Anderson Cancer Center, Houston, TX	USA	p	250	gantry, horiz.	2006	114	Dec-06
FPTI, Jacksonville, FL	USA	p	230	gantry, horiz.	2006	15	Dec-06



# Partikelterapi – planlagte facilliteter

## Particle therapy facilities in a planning stage or under construction:

WHO, WHERE	COUNTRY	PARTICLE	MAX. CLINICAL ENERGY (MeV)	BEAM DIRECTION	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
RPTC, Munich*	Germany	p	250 SC cyclotron	4 gantries, with scanning, 1 horiz.	5	2007
PSI, Villigen*	Switzerland	p	250 SC cyclotron	Additional gantry, 2D parallel scanning, 1 horiz.	3	2007/08 (OPTIS2/ Gantry2 )
NCC, Seoul*	Korea	p	230 cyclotron	2 gantries 1 horiz.	3	End of 2007
UPenn*	USA	p	230 cyclotron	4 gantries 1 horiz.	5	2009
Med-AUSTRON	Austria	p, ion	synchrotron	2 gantries? 1-2 horiz.	3-4?	2011?
Trento	Italy	p	? cyclotron	1 gantry 1 horiz.	2	2010?
CNAO, Pavia*	Italy	p, ion	430/u synchrotron	1 gantry? 3 horiz. 1 vert	3-4	2009?
Heidelberg/GSI Darmstadt*	Germany	p, ion	430/u synchrotron	1 gantry, raster scanning, 2 fixed beams	3	2008
iThemba Labs	South Africa	p	230 cyclotron	1 gantry 2 horiz.	3	2009?
RPTC, Koeln	Germany	p	250 SC cyclotron	4 gantries 1 horiz.	5	?
WPE, Essen*	Germany	p	230 cyclotron	3 gantries 1 horiz.	4	2009
CPO, Orsay*	France	p	230 cyclotron	1 gantry, 4 fixed beams	3	2010
PTC, Marburg*	Germany	p, ion	430/u synchrotron	3 horiz. fixed beams, 1 45 degrees fixed beam	4	2010
Northern Illinois PT Res.Institute, W. Chicago, IL	USA	p	250 accelerator	2-3 gantries, 1-2 horiz.	4	2011







*(Uppsala, Sweden)*

Ældre partikeltarapi faciliteter  
forbundet med et fysik-institut.

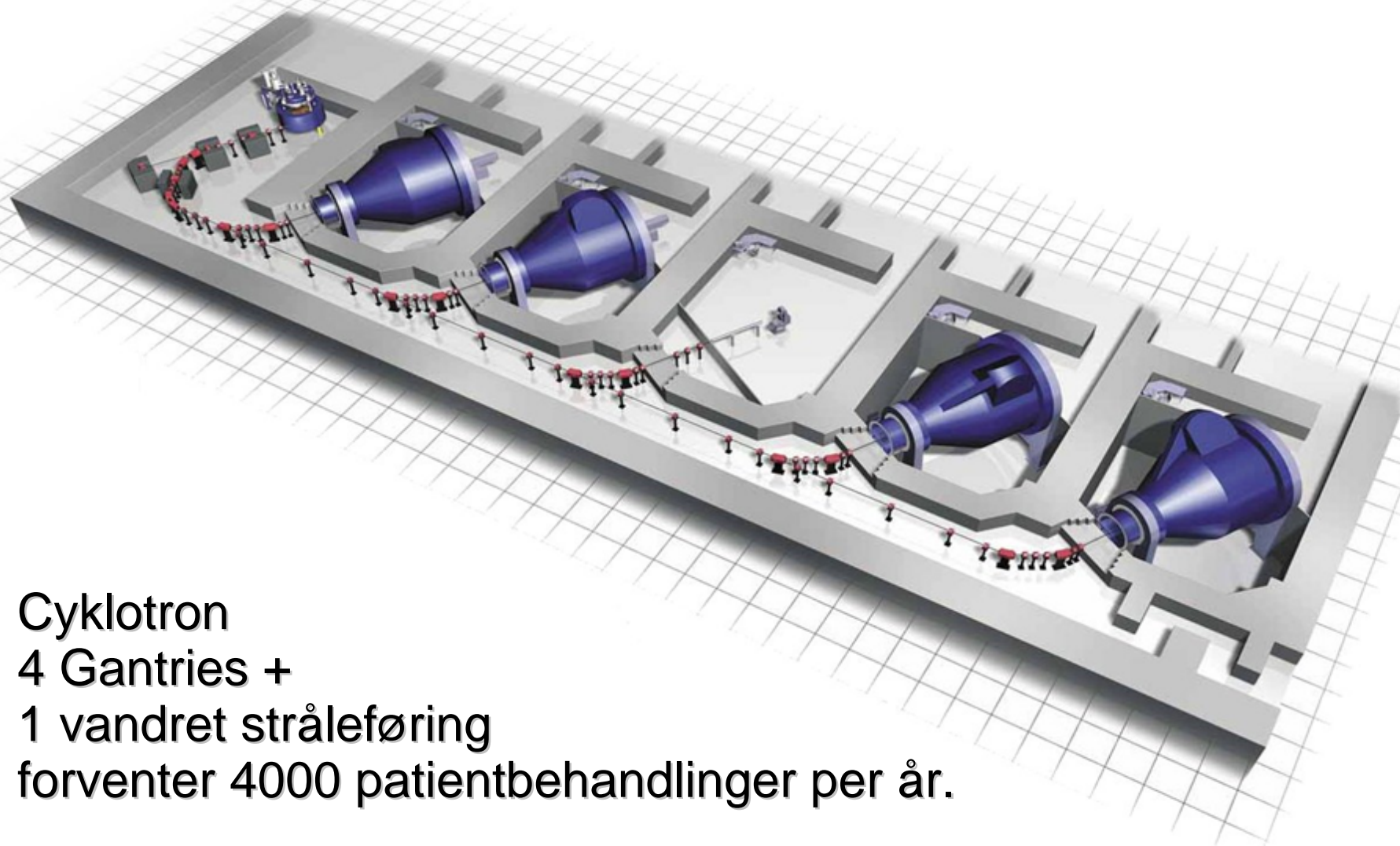
Behandlingsrum ligner mere et  
fysiklaboratorium. (og det er det også)



Eksempel på moderne protonterapifacilitet:

*Rinecker Proton Therapy Center (RPTC-1)*

# Protonterapi – RPTC Munich



Cyklotron  
4 Gantries +  
1 vandret stråleføring  
forventer 4000 patientbehandlinger per år.

(ACCEL)



# Protonterapi – RPTC München



Superledende cyklotron

max: 250 MeV protoner

(rptc.de)

# Protonterapi – RPTC München



Stråleføring fra cyklotron til de 5 behandlingsrum. (Beam føres kun til et af rummene ad gangen.)

(rptc.de)



(rptc.de)

4 Isocentriske proton gantries,

# Protonterapi – RPTC München



(rptc.de)

*RPTC gantry nozzle*

Planlagt også i Köln og Leipzig.

Røntgen-guided fuldautomatisk patient positionering.

2x MR scannere

2x kombinerede PET-CT scannere

”Full body staging examination”, (~360 5 mm slices), lokaliserer tumorer og metastaser

Fx. lungetumorer. Med bedøvelse bliver åndedrættet afbrudt under bestråingen (isf. ”gating”), for at undgå positioneringsfejl.

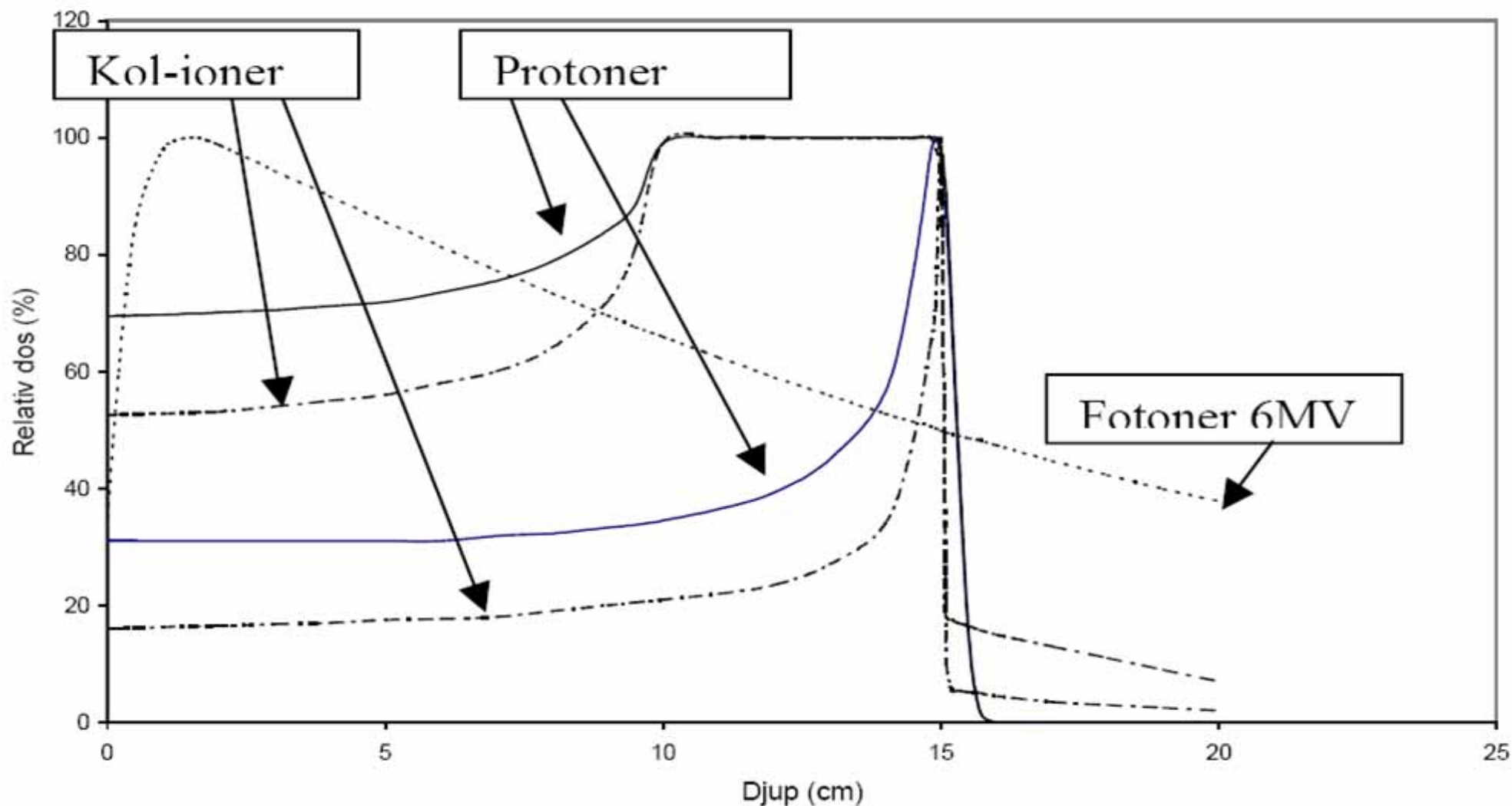
Anslået pris per komplet behandling ink. diagnose: 17.500 €



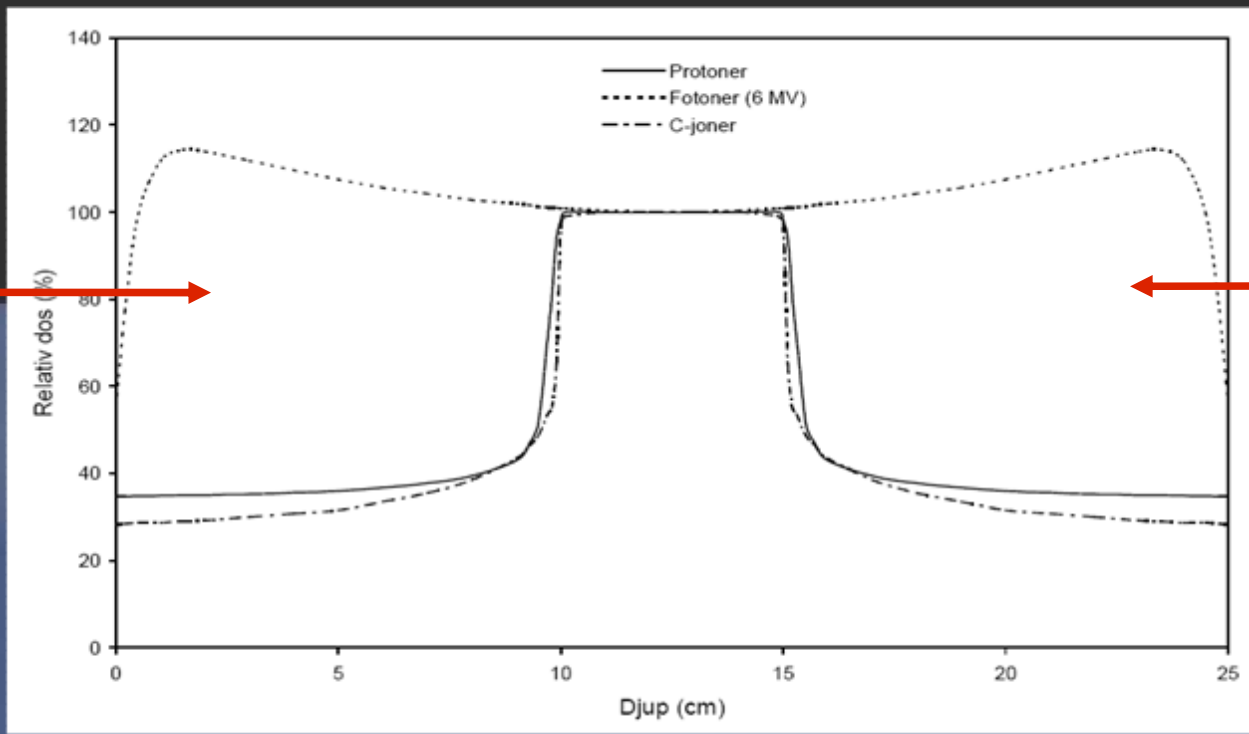
Tunge ioner  
(dvs.: tungere end protoner)



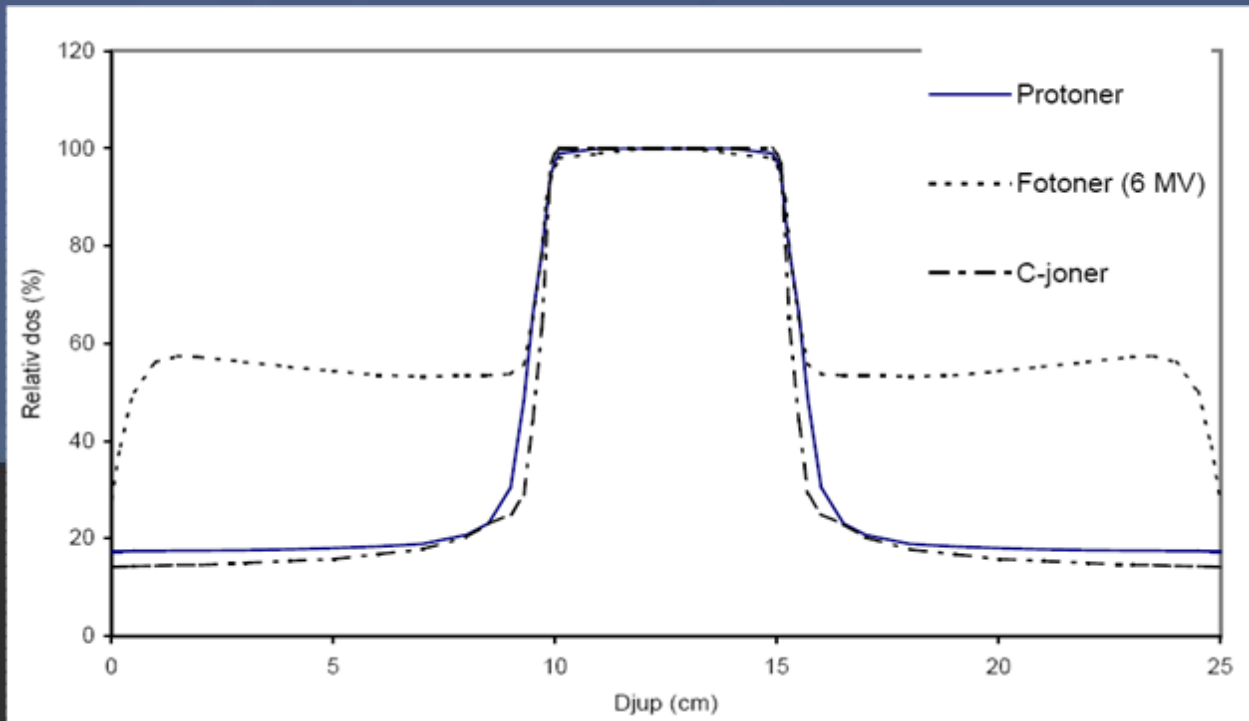
# Fotoner vs. Protoner vs. Kul-ioner



(SPTC, "Val av utrustning för strålbehandling med protoner, slutrapport 2003-010-05)



To opponerende  
felter



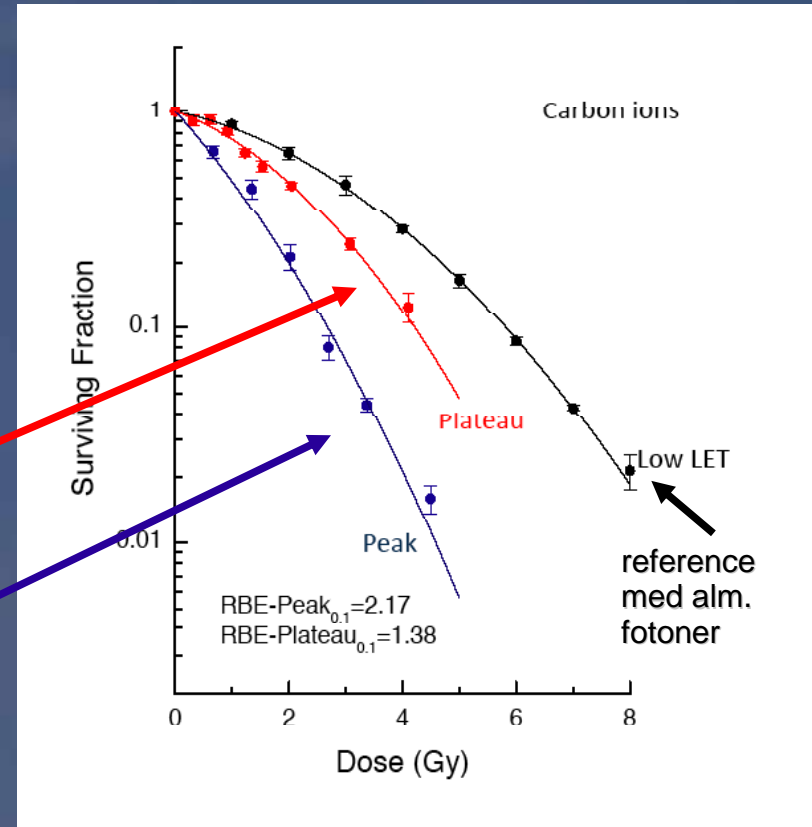
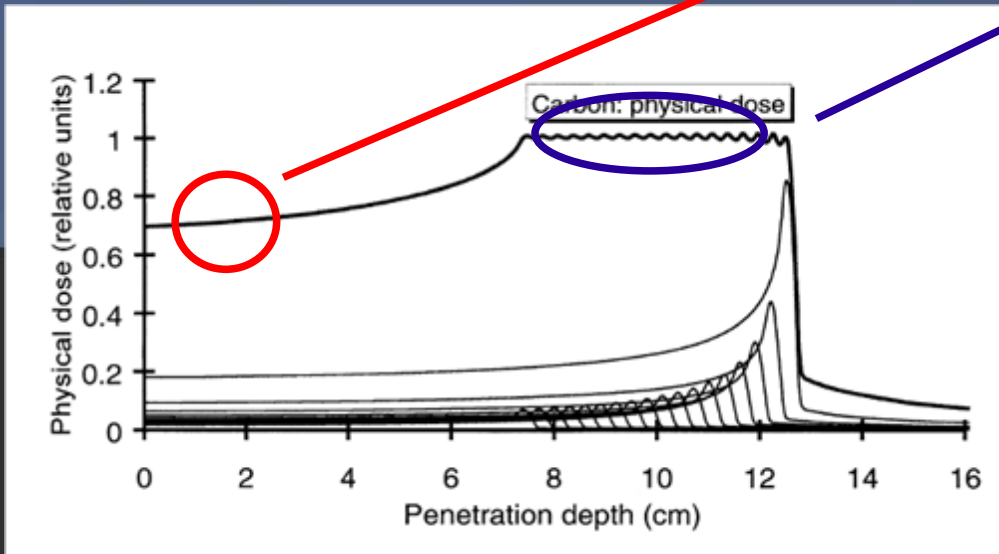
fire felter

(SPTC, "Val av utrustning för strålbehandling med protoner, slutrapport 2003-010-05)

Men hvad er så forskellen mellem Kulioner og protoner?

Radiobiologien!

Samme fysisk dosis for fotoner (eller protoner) og for kulioner, gør ikke samme biologiske skade.



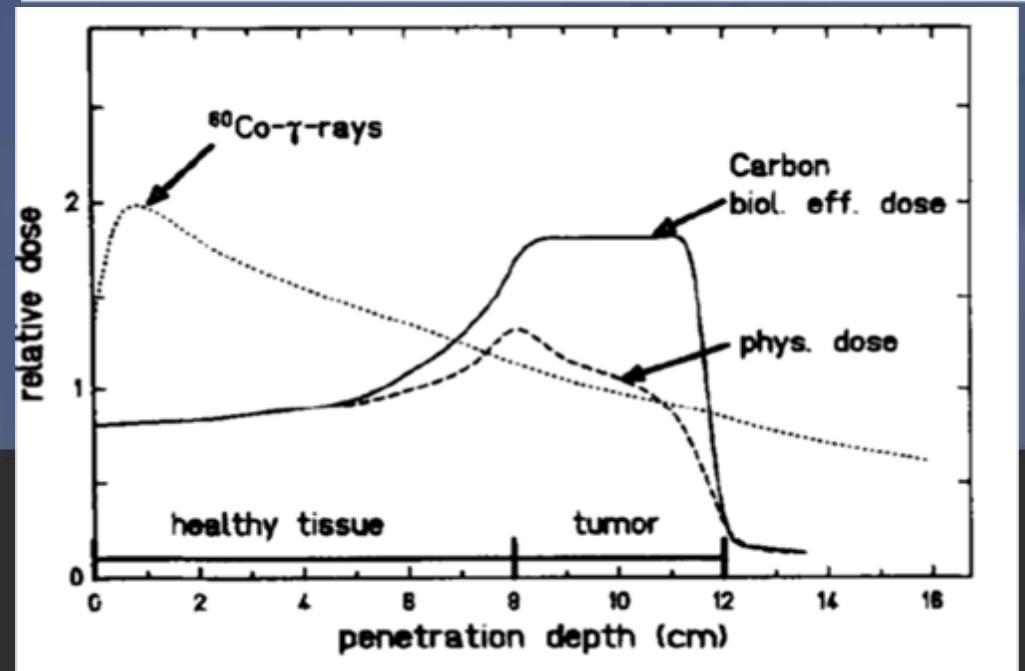
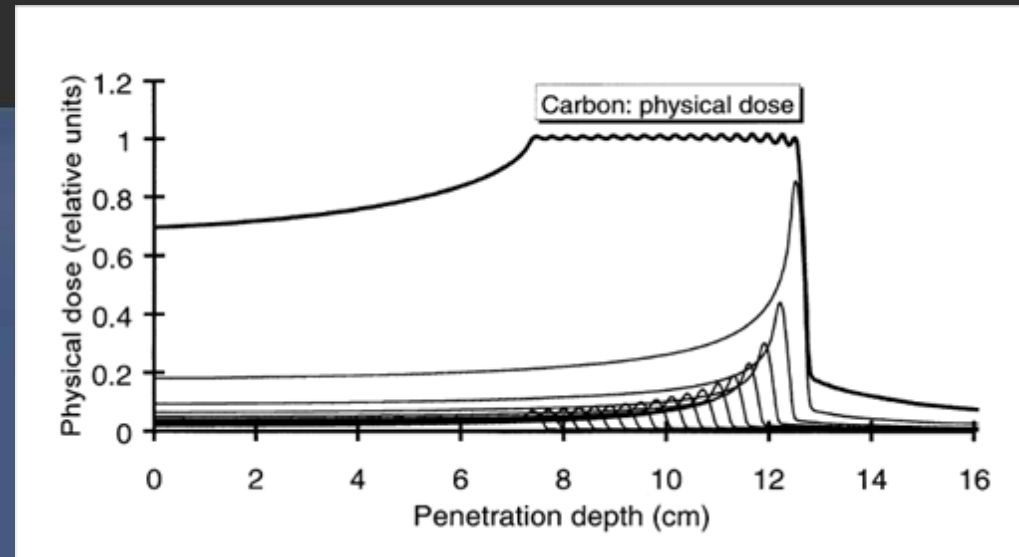
# Kulioner - Radiobiologi

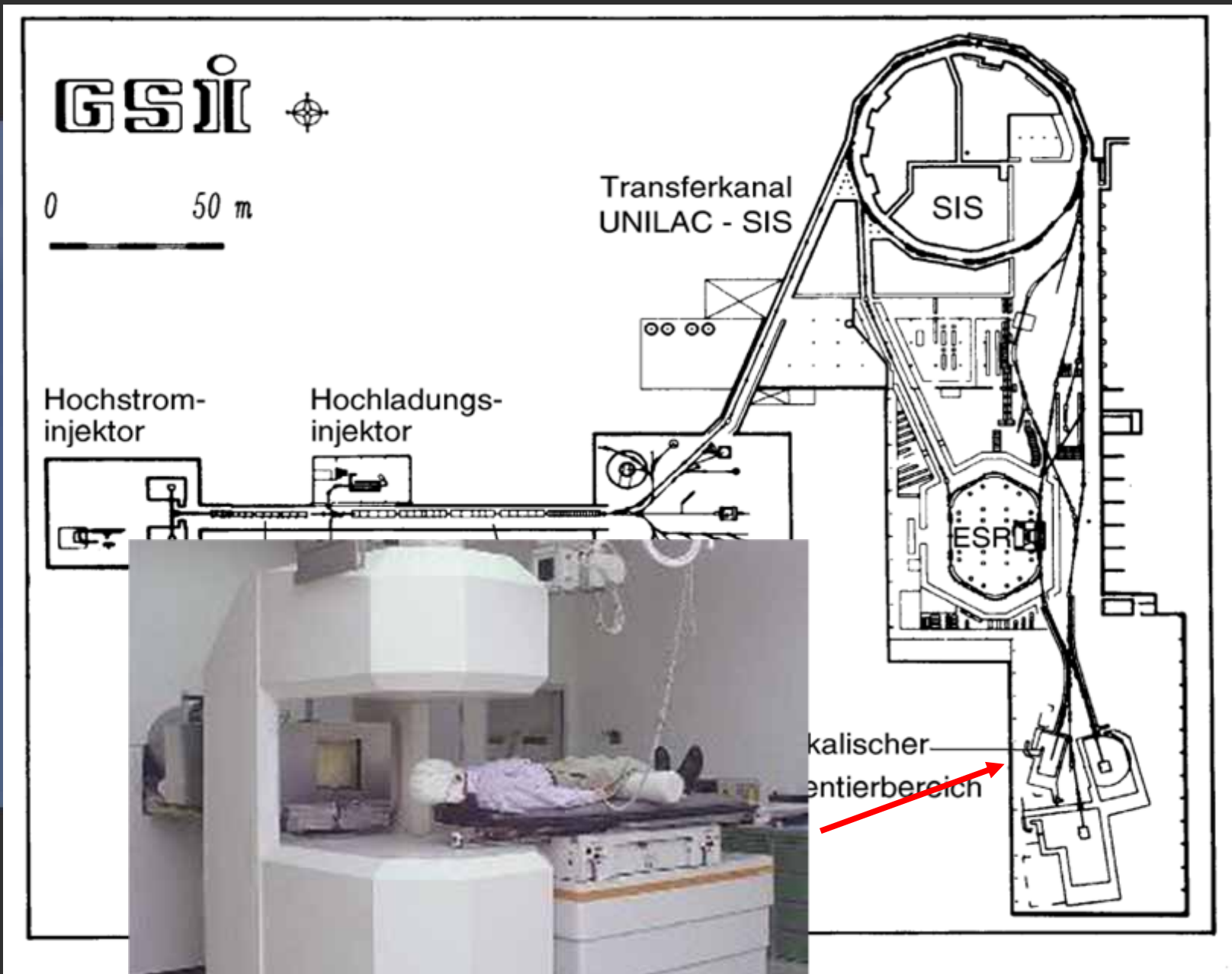
Derfor: ikke nok at se på fysisk dosis.

Inkluder radiobiologi, optimer dosisplan efter **biologisk effektiv dosis**.

Den væsentlige forskel er i radiobiologien: radioresistente tumorer rammes nemmere med kulioner der har høj RBE.

.. og der forskes....

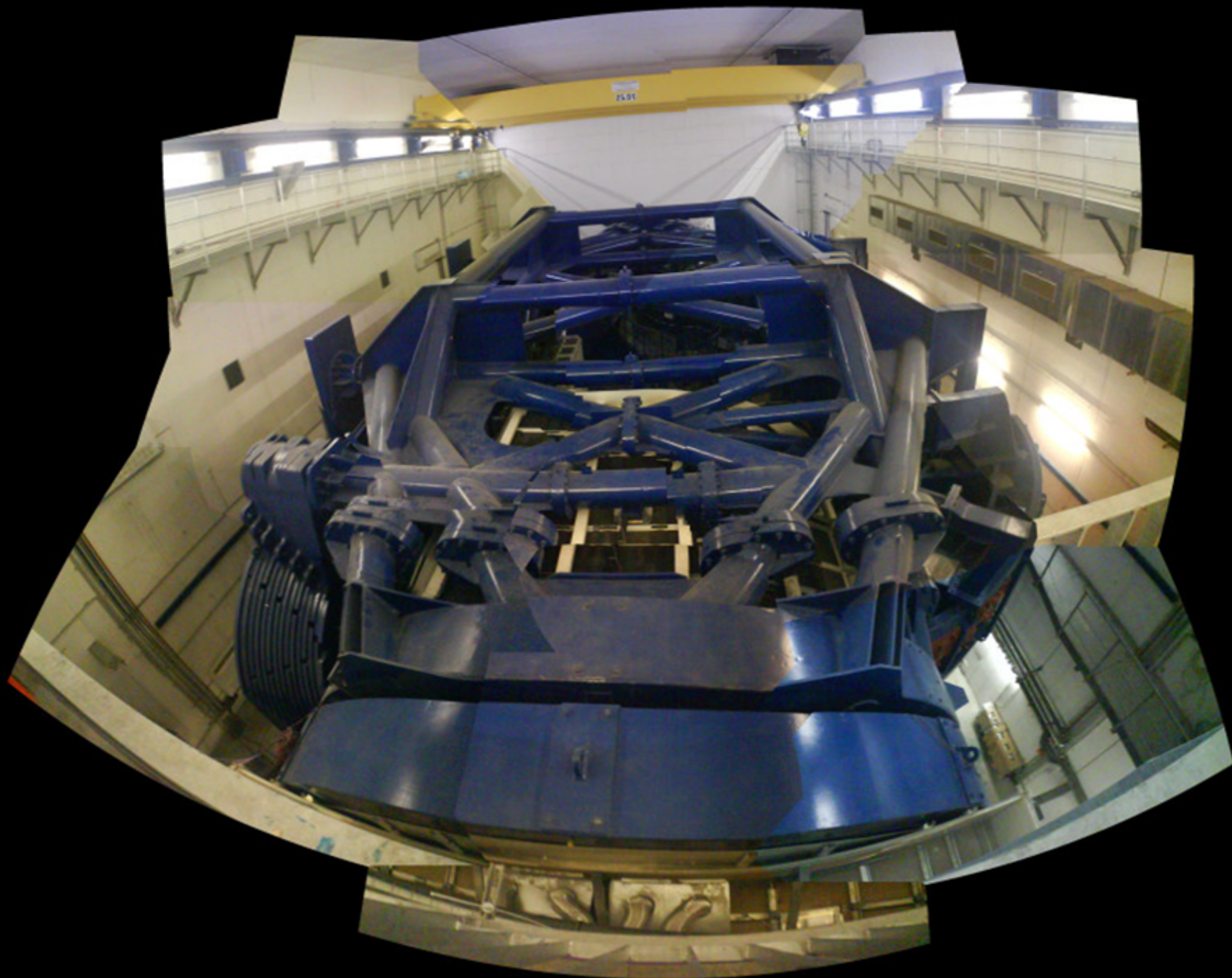


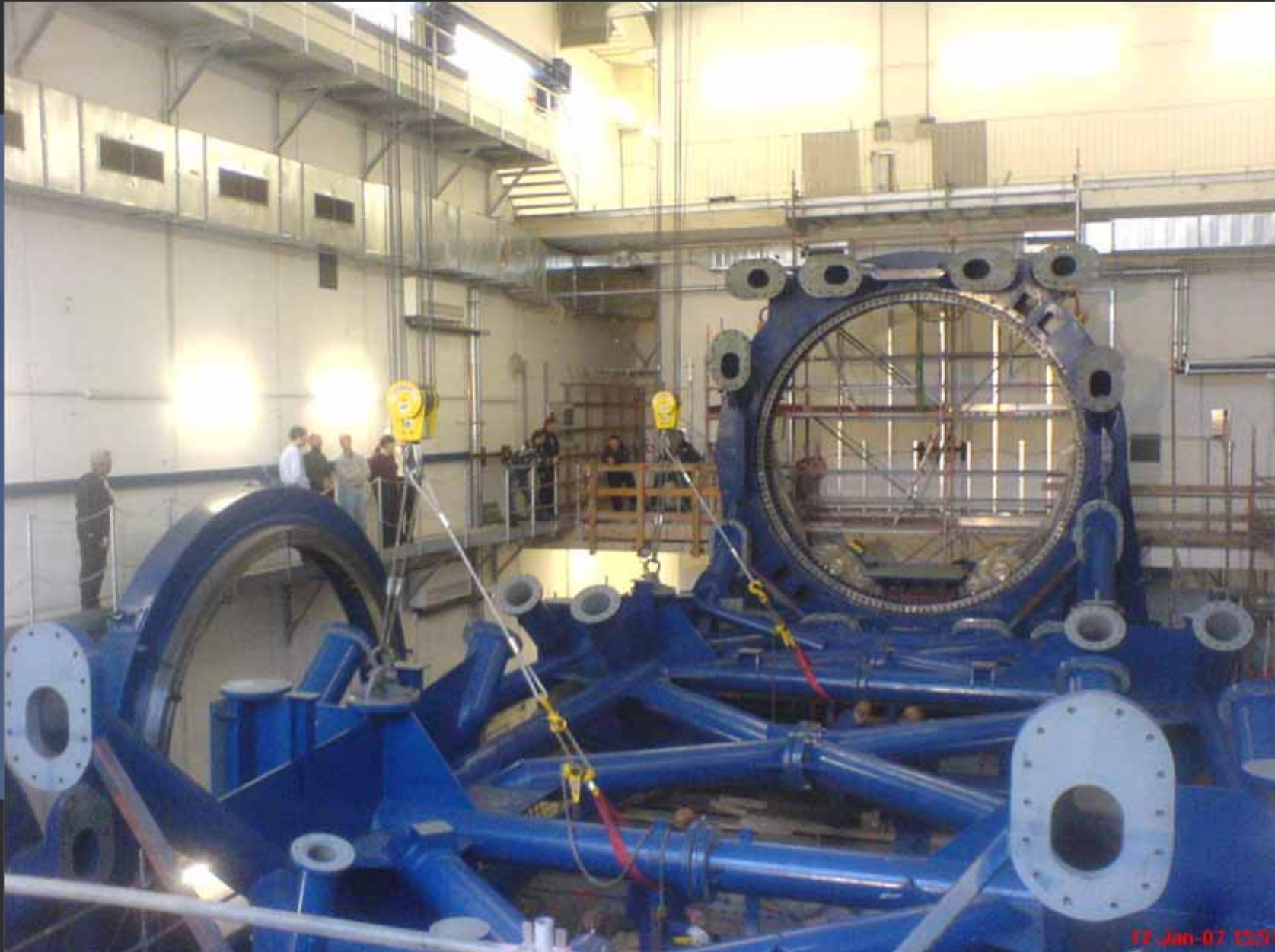


(gsi.de.)



lipole)





(O. Jäkel)

17 Jan-07 15:51



So groß wie ein halbes Fußballfeld

# Deutsche bauen Strahlenkanone gegen KREBS



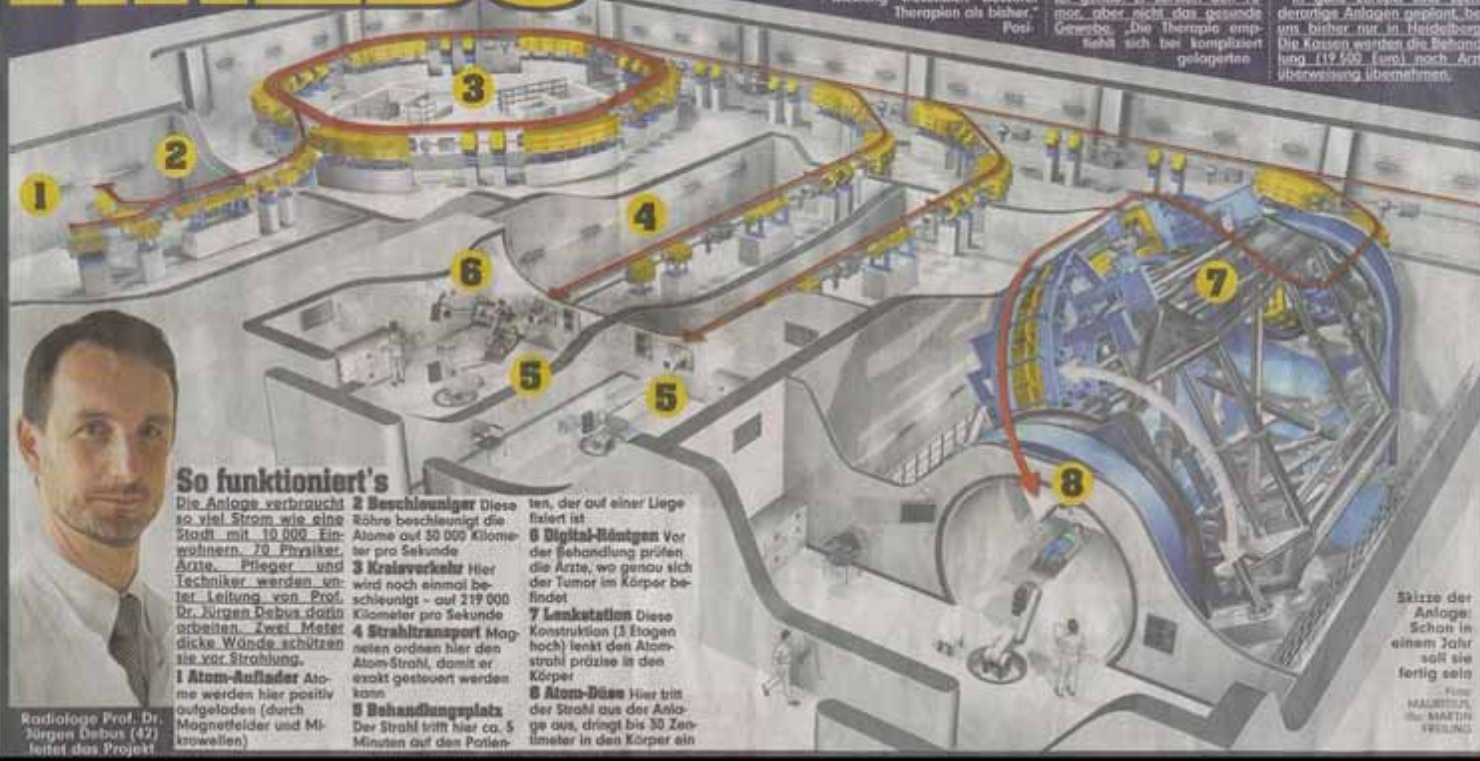
Krebszellen wie diese werden durch den Atomstrahl zerstört.

Heidelberg - Sie ist halb so groß wie ein Fußballfeld und verbraucht so viel Strom wie eine Kleinstadt. Doch sie ist die größte Hoffnung für Krebskranke! An der Uni Heidelberg bauen deutsche For-

scher eine Strahlenkanone, die Tumore einfach wegscleift. Ende 2007 können die ersten Patienten kommen. Radiologe Prof. Dr. Jürgen Debus (47), der das Projekt leitet: „Ein Meilenstein in der Entwicklung wesentlich besserer Therapien als bisher.“ Posi-

tiv geladene Atome werden in der Anlage auf bis zu 219 000 Kilometer pro Sekunde beschleunigt, dann in das kranke Gewebe gelenkt. Durch Magneten wird der Atomstrahl präzise gesteuert - bis auf 0,5 Millimeter genau. Er zerstört den Tumor, aber nicht das gesunde Gewebe. „Die Therapie empfiehlt sich bei komplexen, gelagerten

Tumoren, z. B. in der Schädelbasis oder an der Wirbelsäule“, so der Professor. Auch Krebs tief im Becken (z. B. an der Prostata) kann die Strahlenkanone heilen. Ihre Kraft dringt bis 30 Zentimeter in den Körper. In ganz Europa sind sechs derartige Anlagen geplant, bei uns bisher nur in Heidelberg. Die Kosten werden die Behandlung (19 500 Euro) noch Arztüberweisung übernehmen.



## So funktioniert's

Die Anlage verbraucht so viel Strom wie eine Stadt mit 10 000 Einwohnern. 70 Physiker, Ärzte, Pfleger und Techniker werden unter Leitung von Prof. Dr. Jürgen Debus daran arbeiten. Zwei Meter dicke Wände schützen sie vor Strahlung. **1 Atom-Auflader** Atome werden hier positiv aufgeladen (durch Magnetfelder und Mikrowellen).

**2 Beschleuniger** Diese Röhre beschleunigt die Atome auf 30 000 Kilometer pro Sekunde. **3 Kreisverkehr** Hier wird noch einmal beschleunigt - auf 219 000 Kilometer pro Sekunde. **4 Strahltransport** Magneten ordnen hier den Atomstrahl, damit er exakt gesteuert werden kann. **5 Behandlungsplatz** Der Strahl trifft hier ca. 5 Minuten auf den Patienten,

der auf einer Liege fixiert ist. **6 Digital-Röntgen** Vor der Behandlung prüfen die Ärzte, wo genau sich der Tumor im Körper befindet. **7 Lenkstation** Diese Konstruktion (3 Etagen hoch) lenkt den Atomstrahl präzise in den Körper. **8 Atom-Düse** Hier tritt der Strahl aus der Anlage aus, dringt bis 30 Zentimeter in den Körper ein.

Skizze der Anlage: Schon in einem Jahr soll sie fertig sein. Foto: MÄDDELING/DR. MARTIN FREILING

(Bild Zeitung)



## Økonomi:

- HIT koster ~ 100 M€
- 50 % offentlige kilder, 50 % Heidelberg Universitet
  
- Pris per behandling (flere fraktioner) ~ 20 k€



- Kun et par 100 patienter behandlet med kulioner i Tyskland (GSI), resten i Japan.

Uafklarede spørgsmål:

- hvad er den biologisk effektive dosis?
- er kulioner "bedre" end protoner? For hvilke tumortyper?
- er der sene effekter af behandlingen?

Stråleterapi med kulioner er eksperimentelt.



# Partikelterapi i Danmark?

- 11 – 32 patienter per 100.000 indbyggere
- “I en dansk sammenhæng ville det svare til 1100 til 1750 patienter om året ...”
- “... hvilket skal ses i sammenhæng med at kun 5-10 patienter om året p.t. sendes til protonbehandling i udlandet (fortrinsvis Boston).”

*(Rapport fra DSKO Accelerator Udvalg,  
2004)*

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# -----The Danish Light Ion Therapy Project-----



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Done

Antiprotoner

NYT!



# AD-4/ACE Kollaborationen

estd. 2003.

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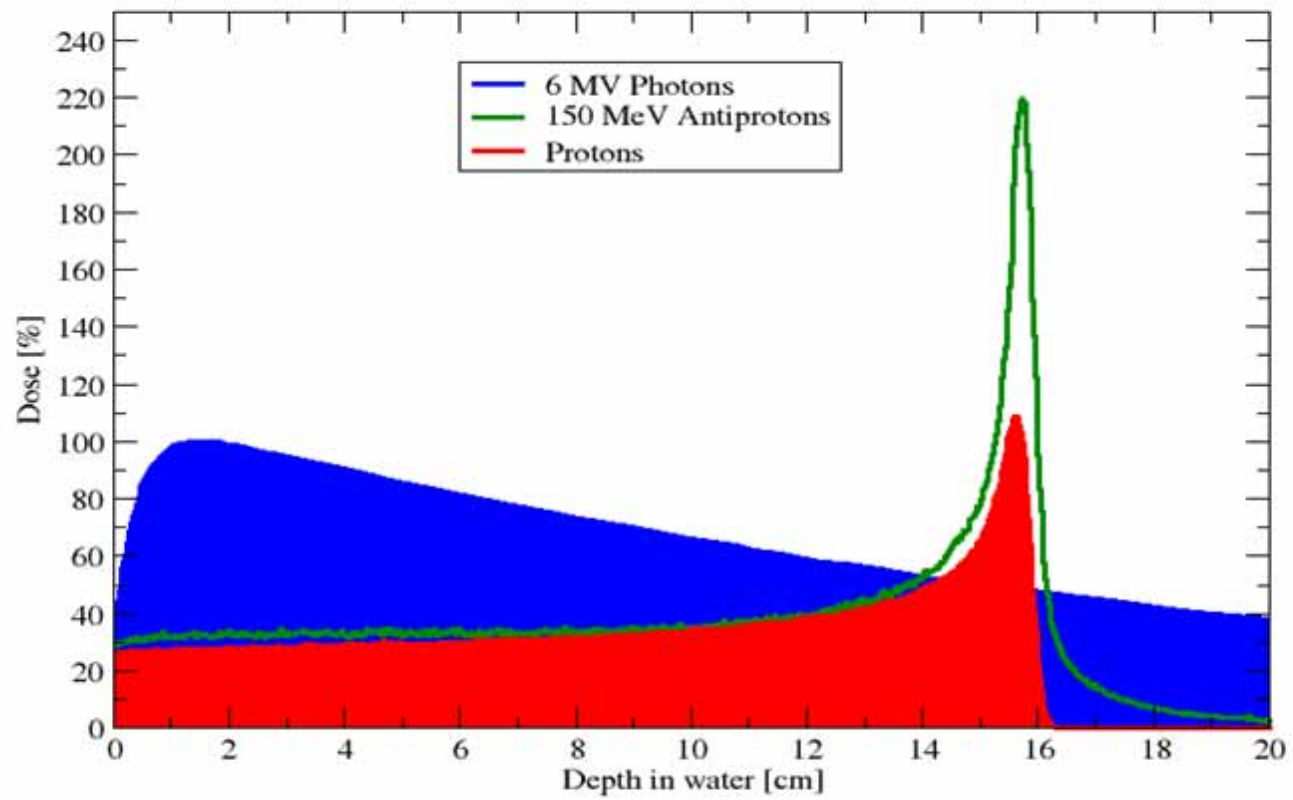
<sup>10</sup> VINCA Institute for Nuclear Sciences, Belgrade, Serbia

<sup>11</sup> University of Maastricht, Res. Institute Growth and Development, The Netherlands.

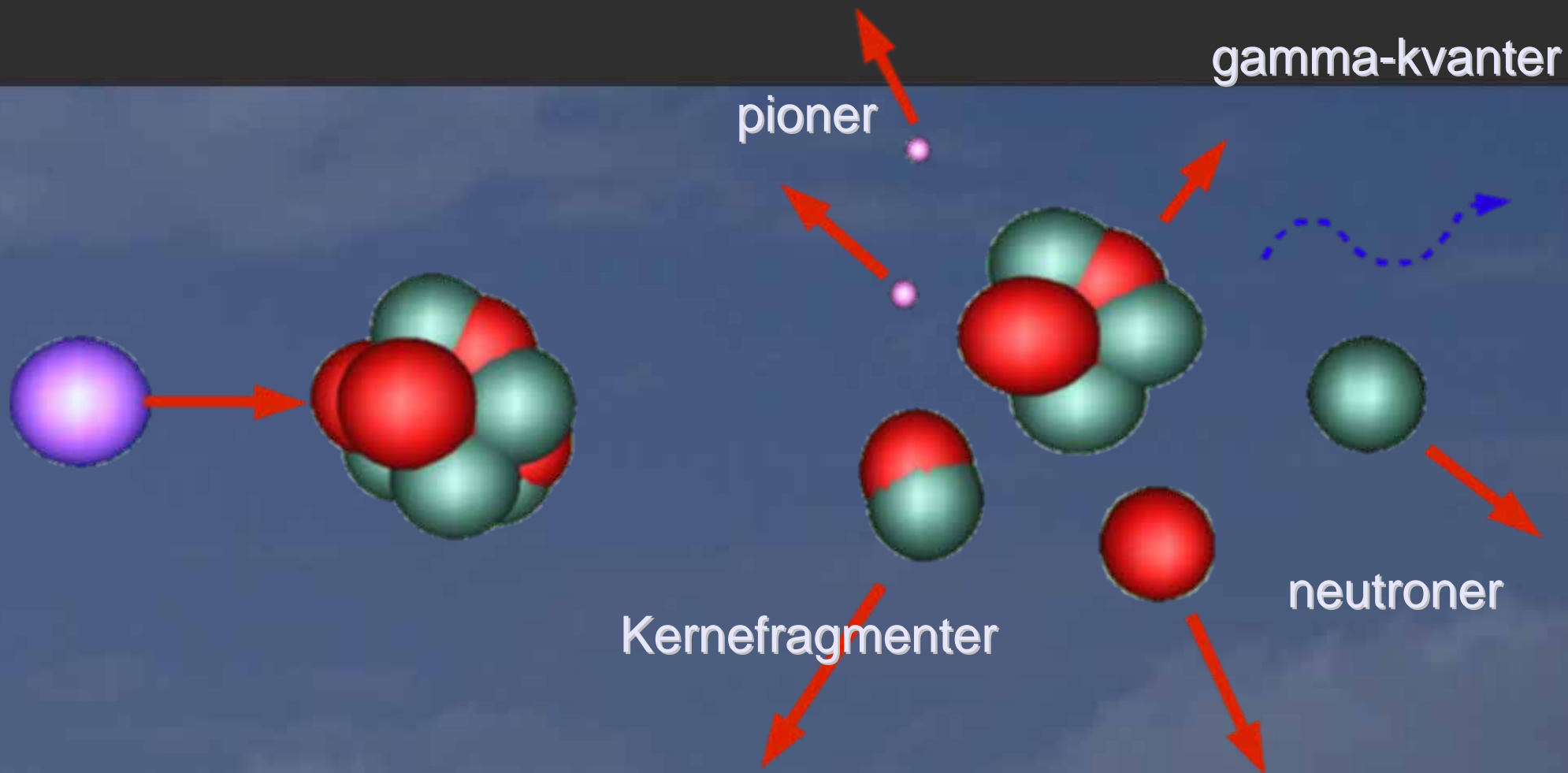
18 participants.

**”Stråleterapi med antiprotoner, gi'r det mening ?”**





# Antiprotoner - Annihilation



- Energi fra annihilation :  $2x m_p \sim 1.88 \text{ GeV}$
- Men langt det meste går tabt med pionerne m.m.
- Kernefragmenter gør lokal skade, dog kun omkring 30 MeV

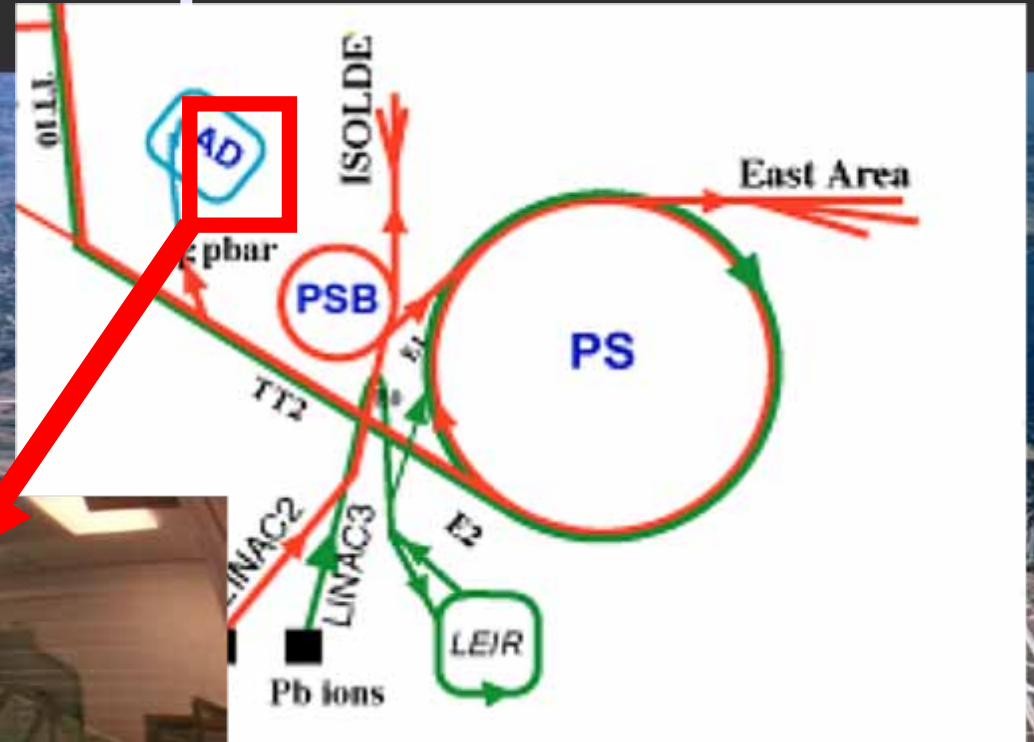


# Antiprotoner - Produktion

Antiproton produktion ved CERN

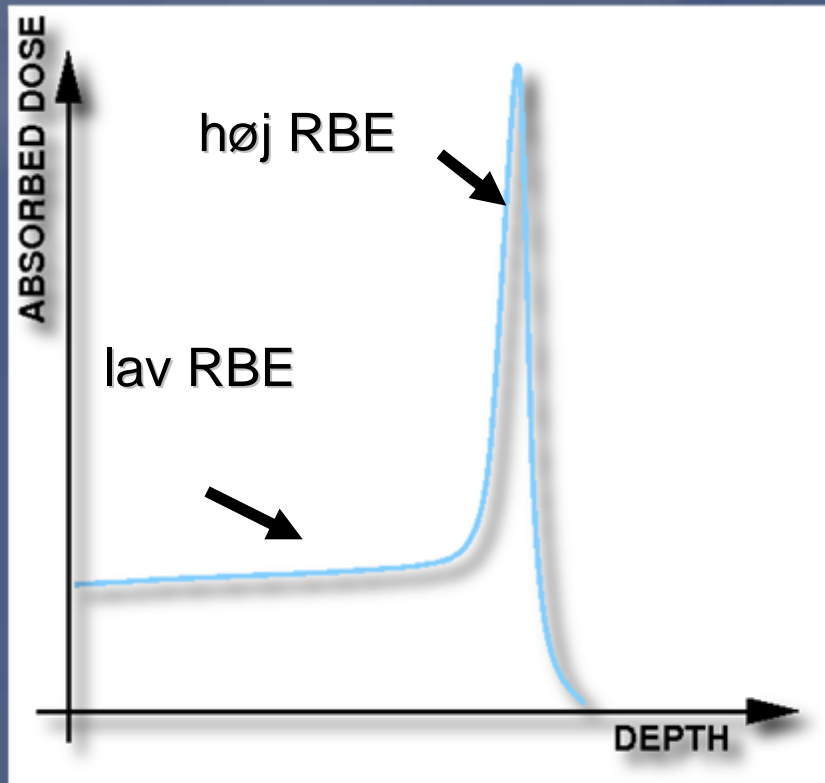
26 GeV protonstråle -> target

$p + p \rightarrow p + p + p + \bar{p}$





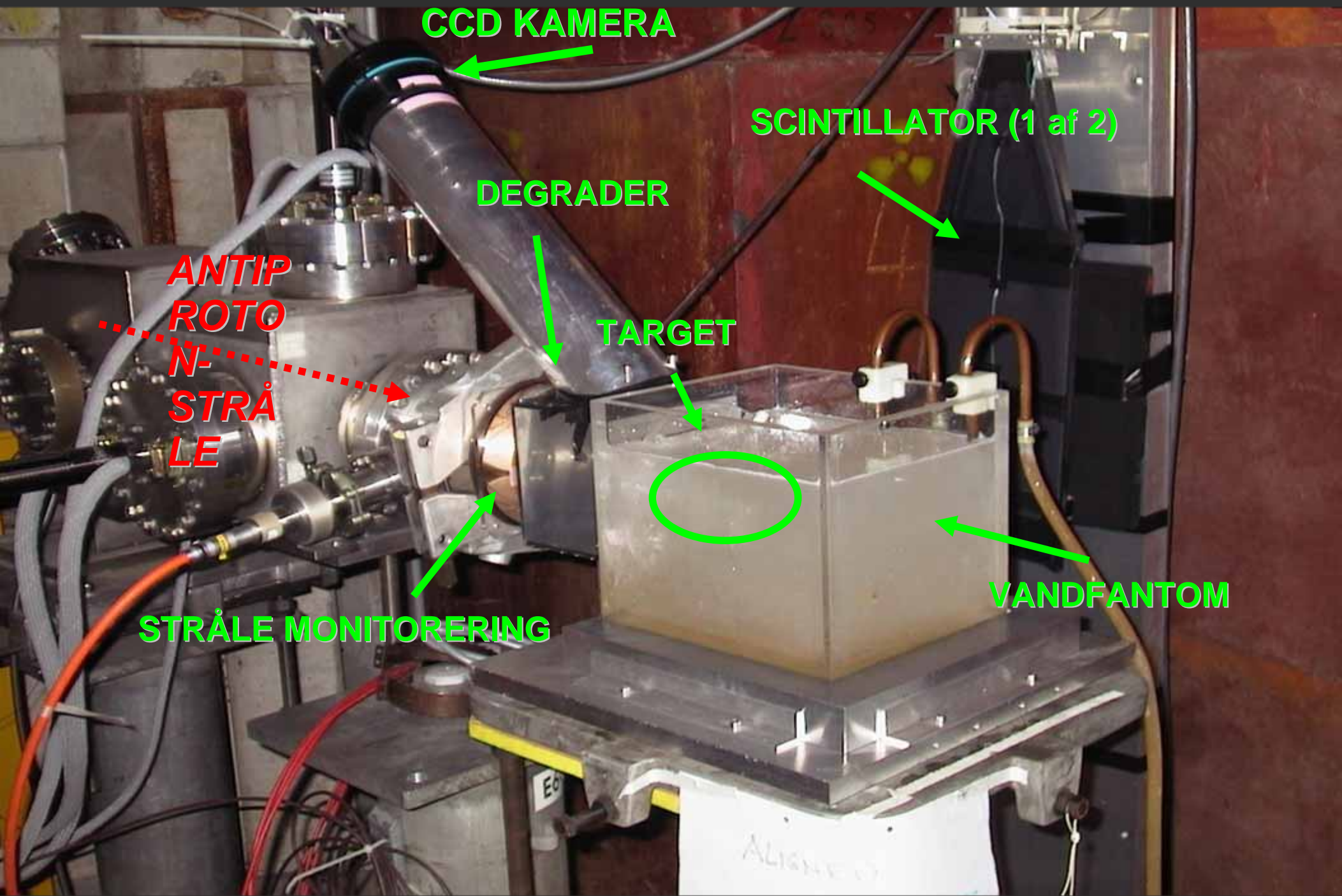
# Antiprotoner - Radiobiologi



Høj RBE i peak, altså meget effekt per dosis...

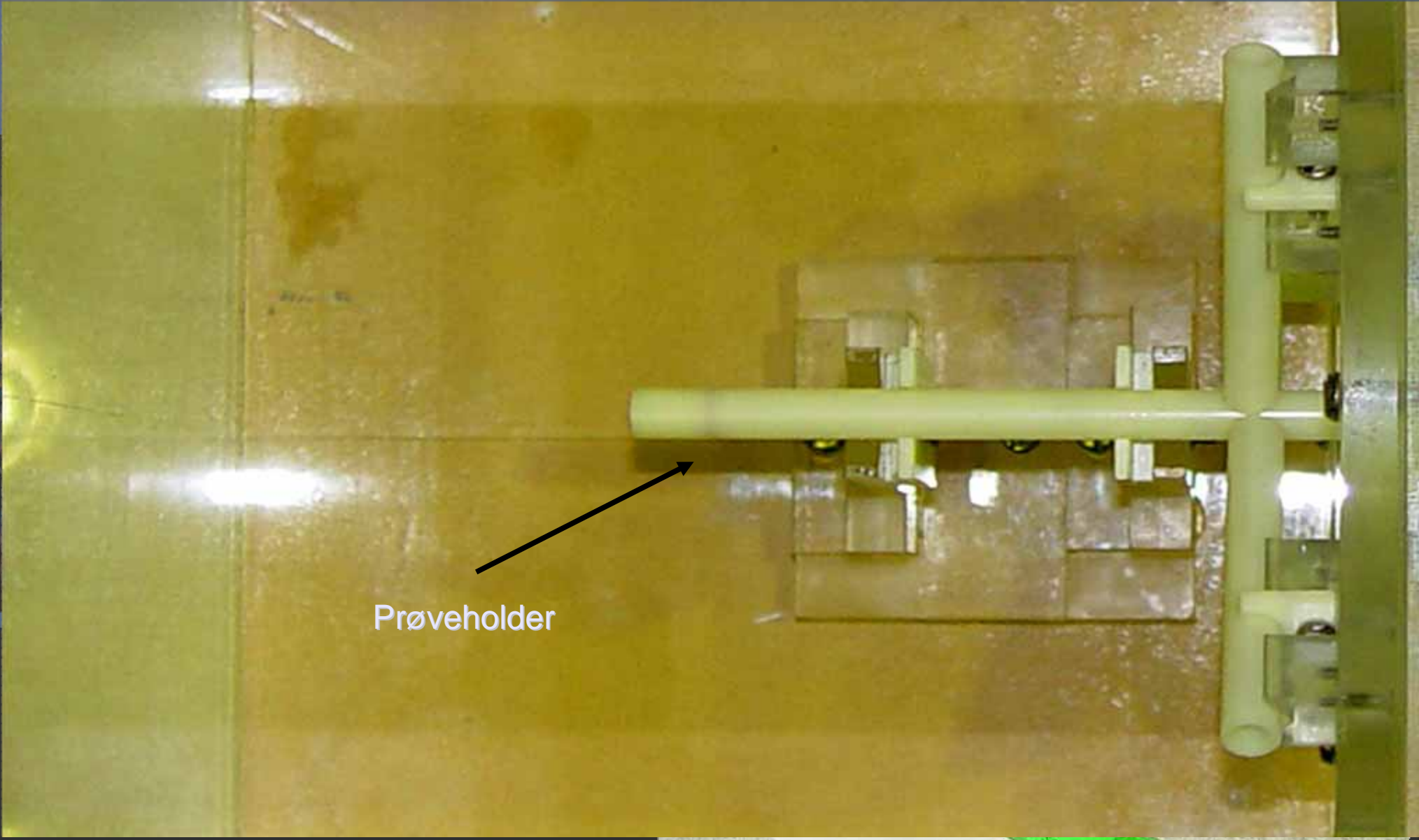
lav RBE i plateau; mindre effekt per dosis.

# AD4/ACE Eksperimentet, CERN



# AD4/ACE Eksperimentet, CERN

Prøveholder



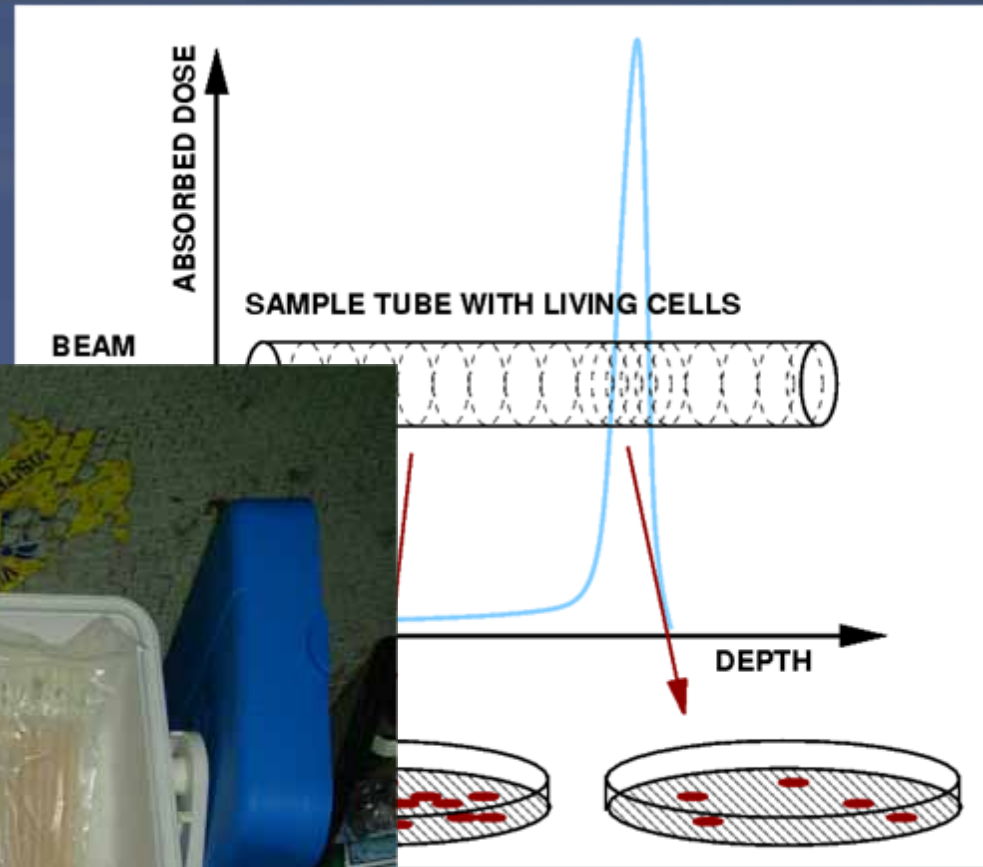


# AD4/ACE - Target

- Kinesiske V79 hamsterceller i gelatine opløsning.

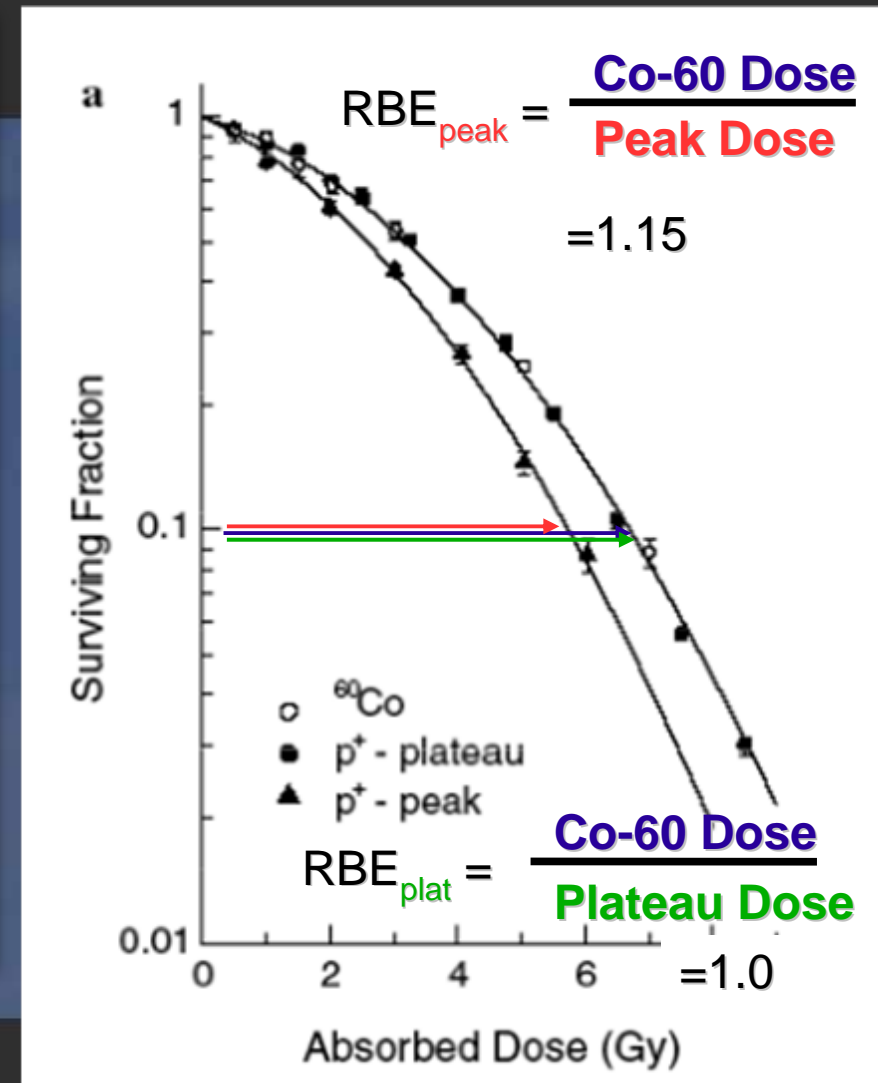
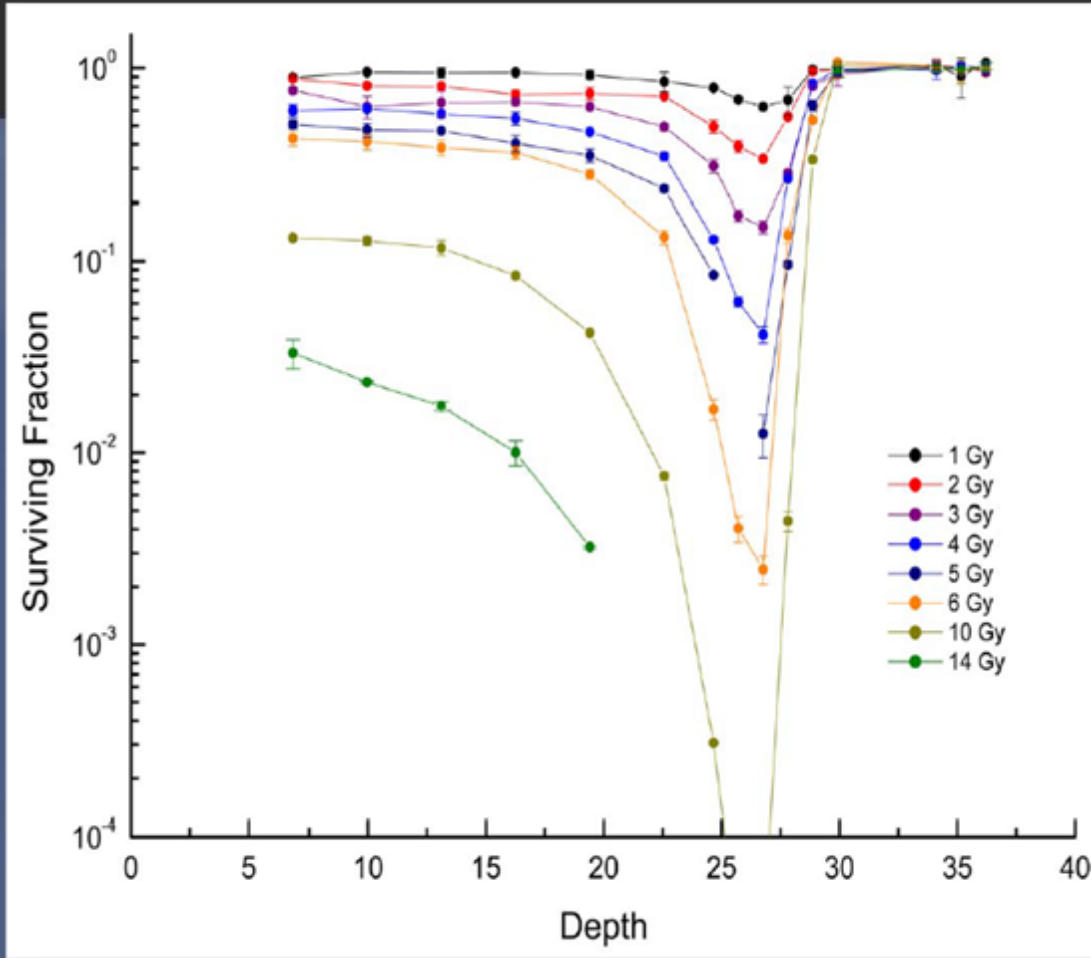
- Kølet ned til et par °C for at stoppe cellereparationer.

- Efter bestråling sættes på Petri-skåle.



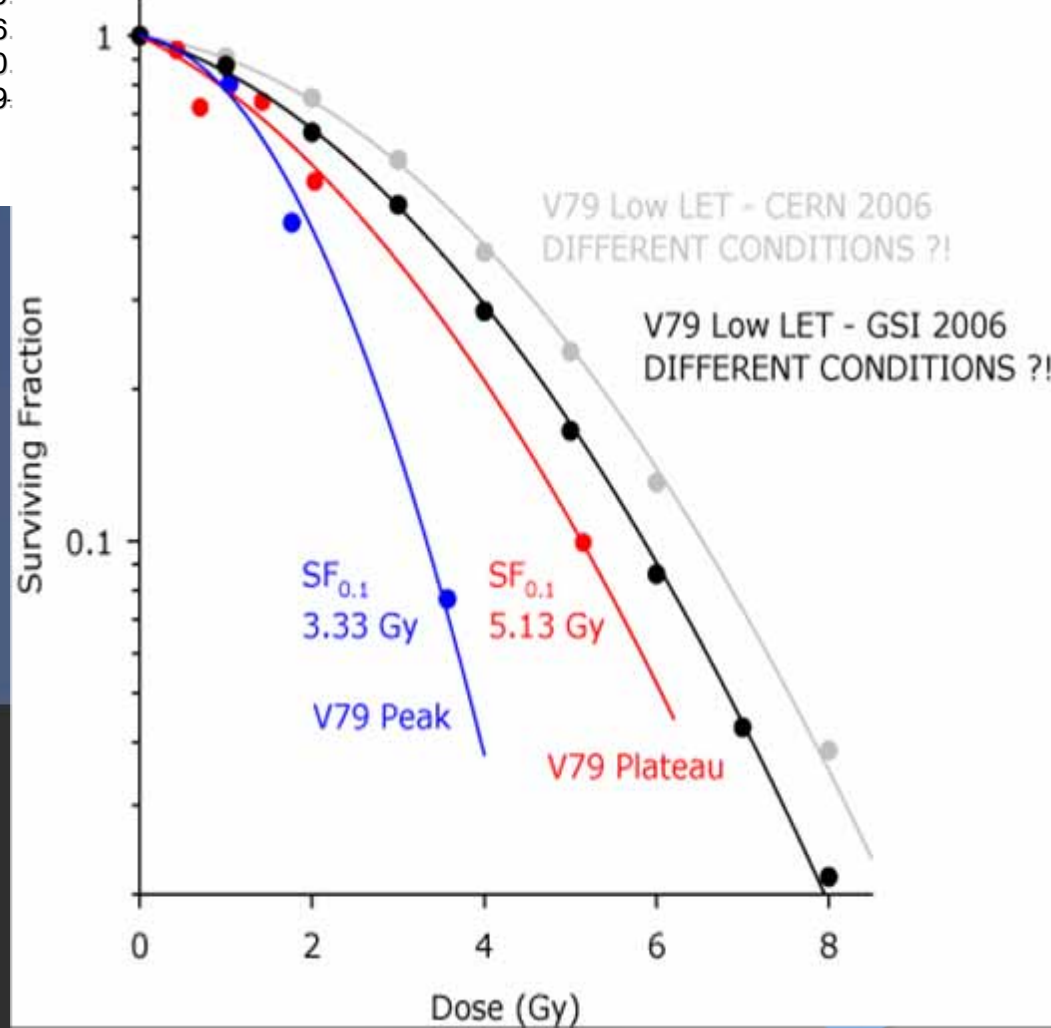
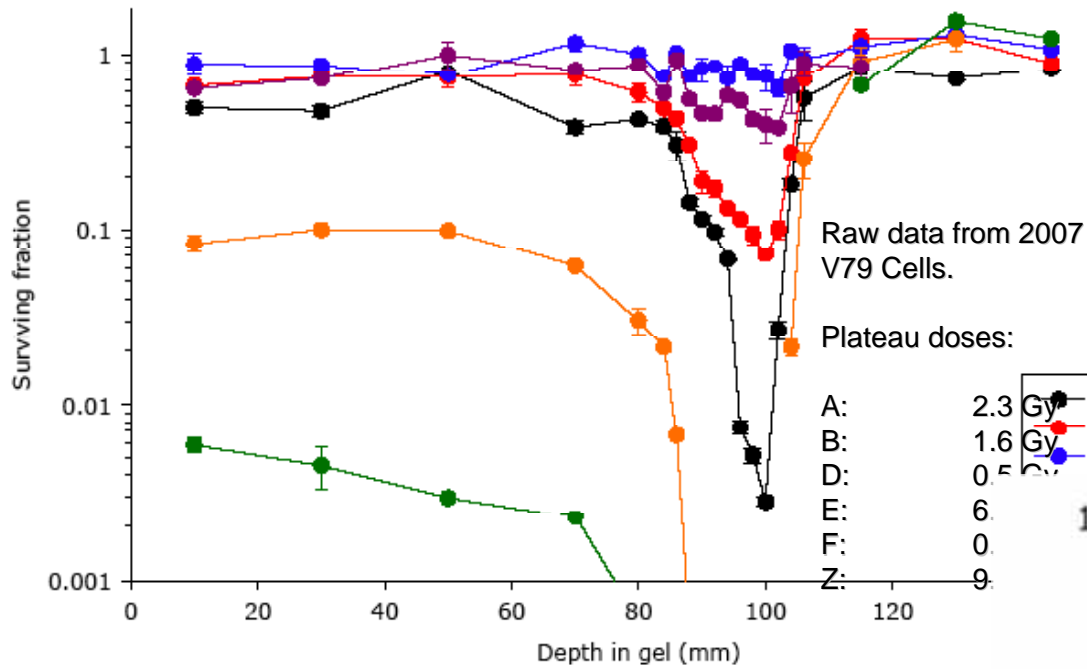


# Relative Biological Efficiency (RBE)



Proton-data fra TRIUMF

# V79 Resultater 2007



RBE(plateau) = 1.15 – 1.27  
RBE(peak) = 1.77 - 1.95

- Bestem den radiobiologiske effekt af antiprotoner, sammenlign med kulioner og protoner.
- Planlægningstudier med antiprotoner, for at sammenligne forskellige partikelterapi.
- Undersøgelser af effekter af bestrålingen, uden for selve antiproton strålen (sekundær cancer induktion)

*Antiprotoner er dyre og vanskelige at fremstille. En dedikeret facillitet kan koste 1 G€ (ca ¼ metro-ring).*

# Protoner ved ASTRID





# Protoner ved ASTRID

