University Hospitals Birmingham NHS
NHS Foundation Trust

UNIVERSITY OF BIRMINGHAM

Accelerator neutron sources for BNCT

Perspectives from the last 15 years

ABNS Meeting 2014, INFN Legnaro

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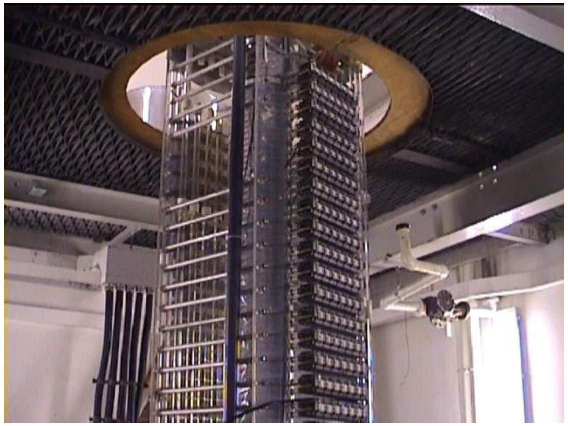
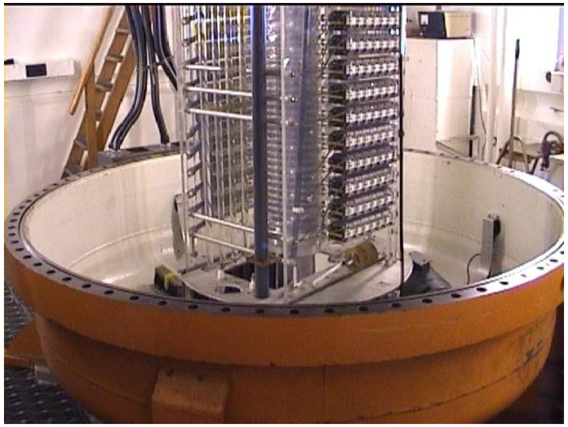
EPSRC
Engineering and Physical Sciences Research Council

Queen Elizabeth Hospital Birmingham Charity

The Birmingham Dynamitron

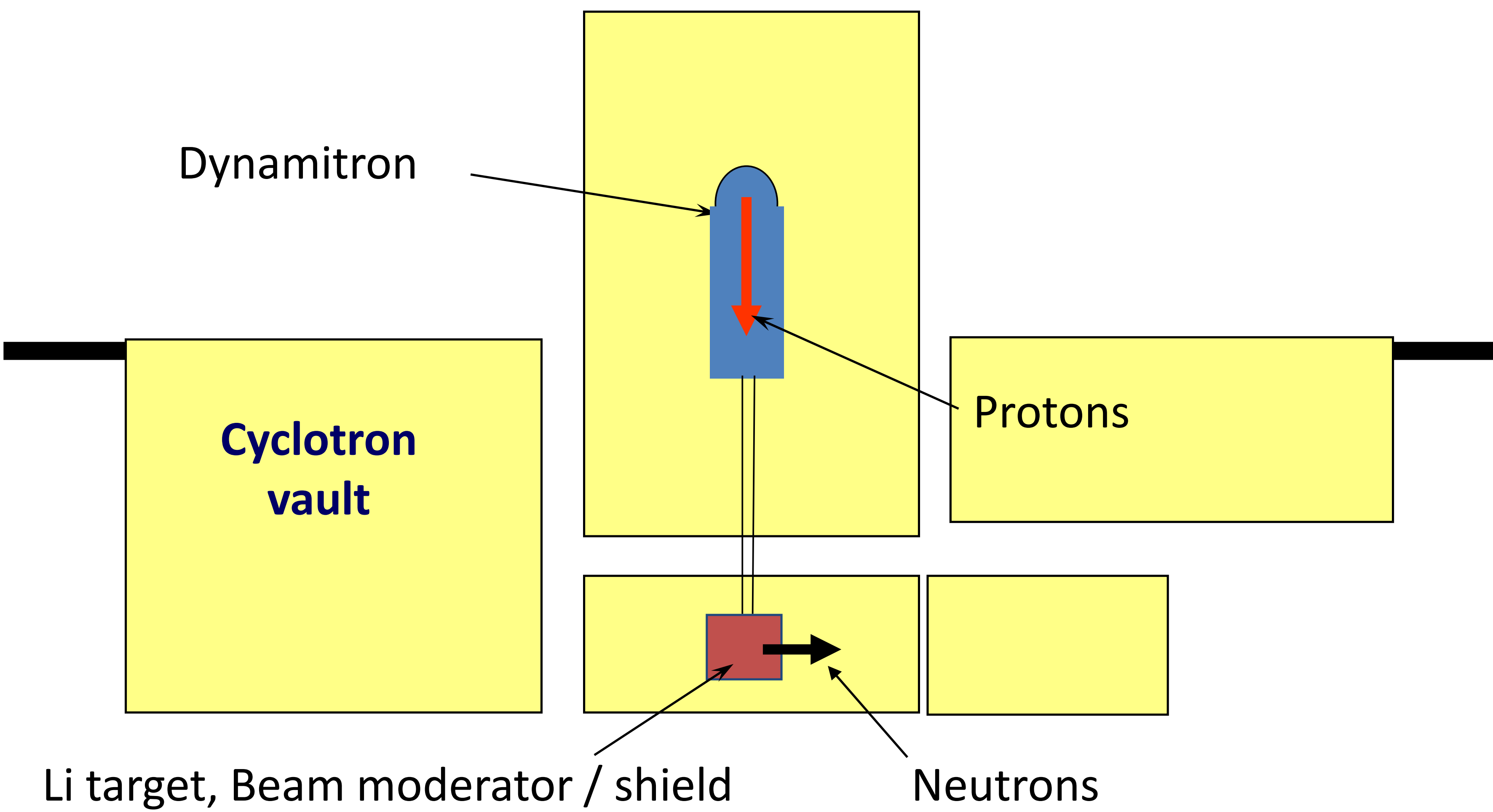
- 3MV maximum energy (2.8MeV used routinely)
- 2mA maximum current from duoplasmatron ion source (1mA used routinely)
- Vertical orientation



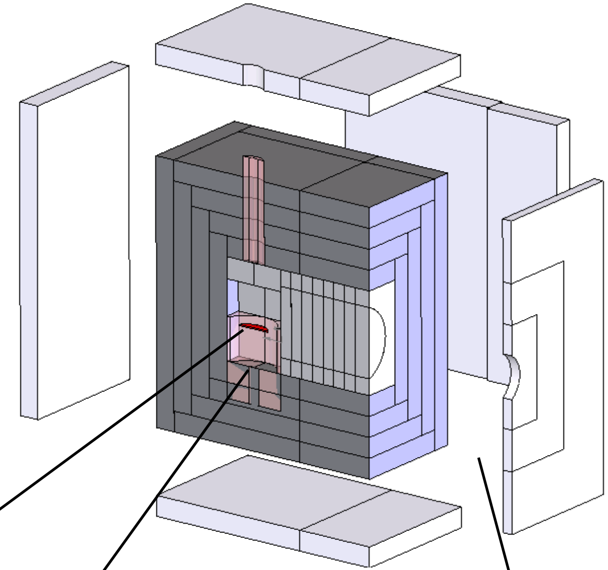


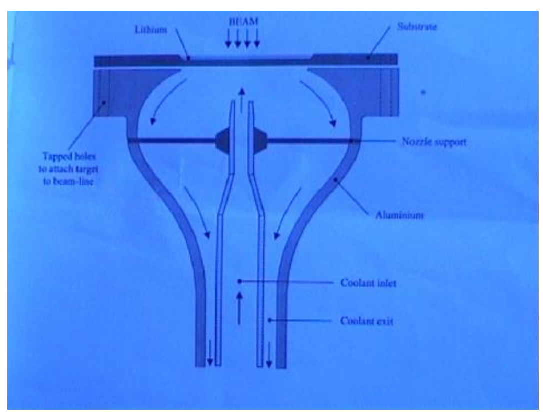
- 15mA ECR ion source available from IBA (should deliver 3mA with current rf oscillator)

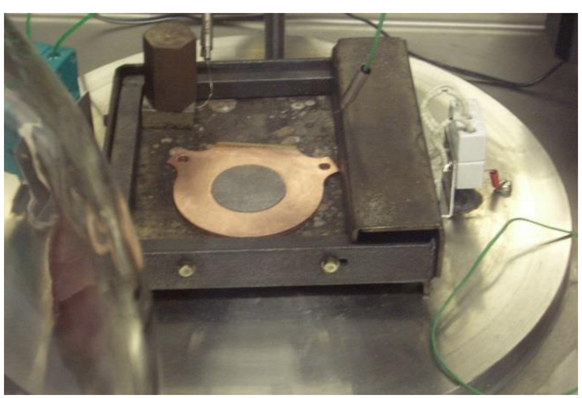
The Medical Physics Building in Birmingham

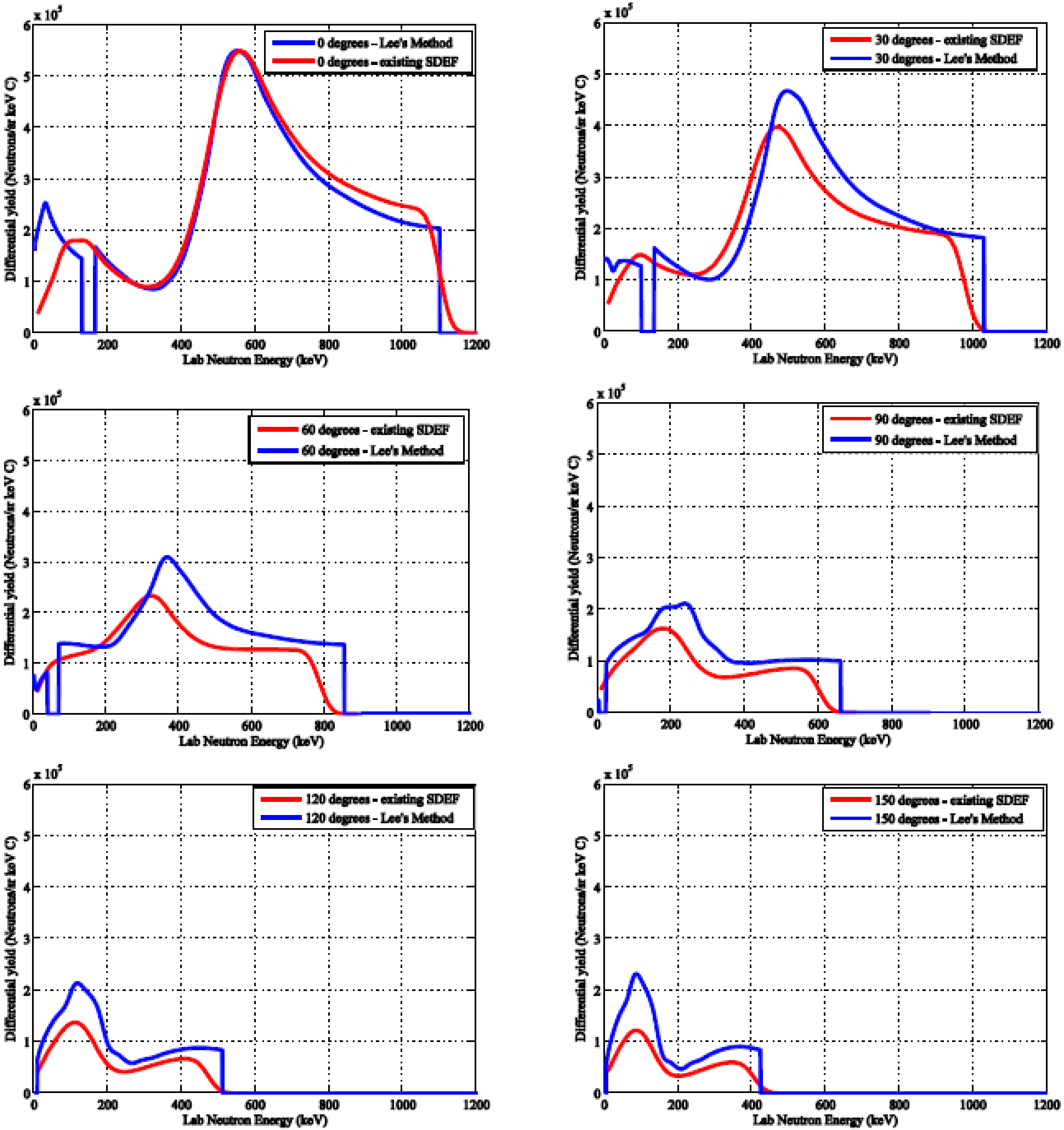


- Solid Li target, 38 mm diameter and 0,7 mm thick (< 1cm^3 Li)
- Neutron source is > 1 x 10^{12} s^{-1} (1 mA proton current at 2.8 MeV)
- Orthogonal design, so maximum neutron energy towards patient is 700 keV









0 degrees – Lee's Method
0 degrees – existing SDEF
30 degrees - existing SDEF
30 degrees - Lee's Method
60 degrees - existing SDEF
60 degrees - Lee's Method
90 degrees - existing SDEF
90 degrees - Lee's Method
120 degrees - existing SDEF
120 degrees - Lee's Method
150 degrees - existing SDEF
150 degrees - Lee's Method
x 10^5
Differential yield (Neutrons/sr keV C)
Lab Neutron Energy (keV)

Decisions that took us to this…..

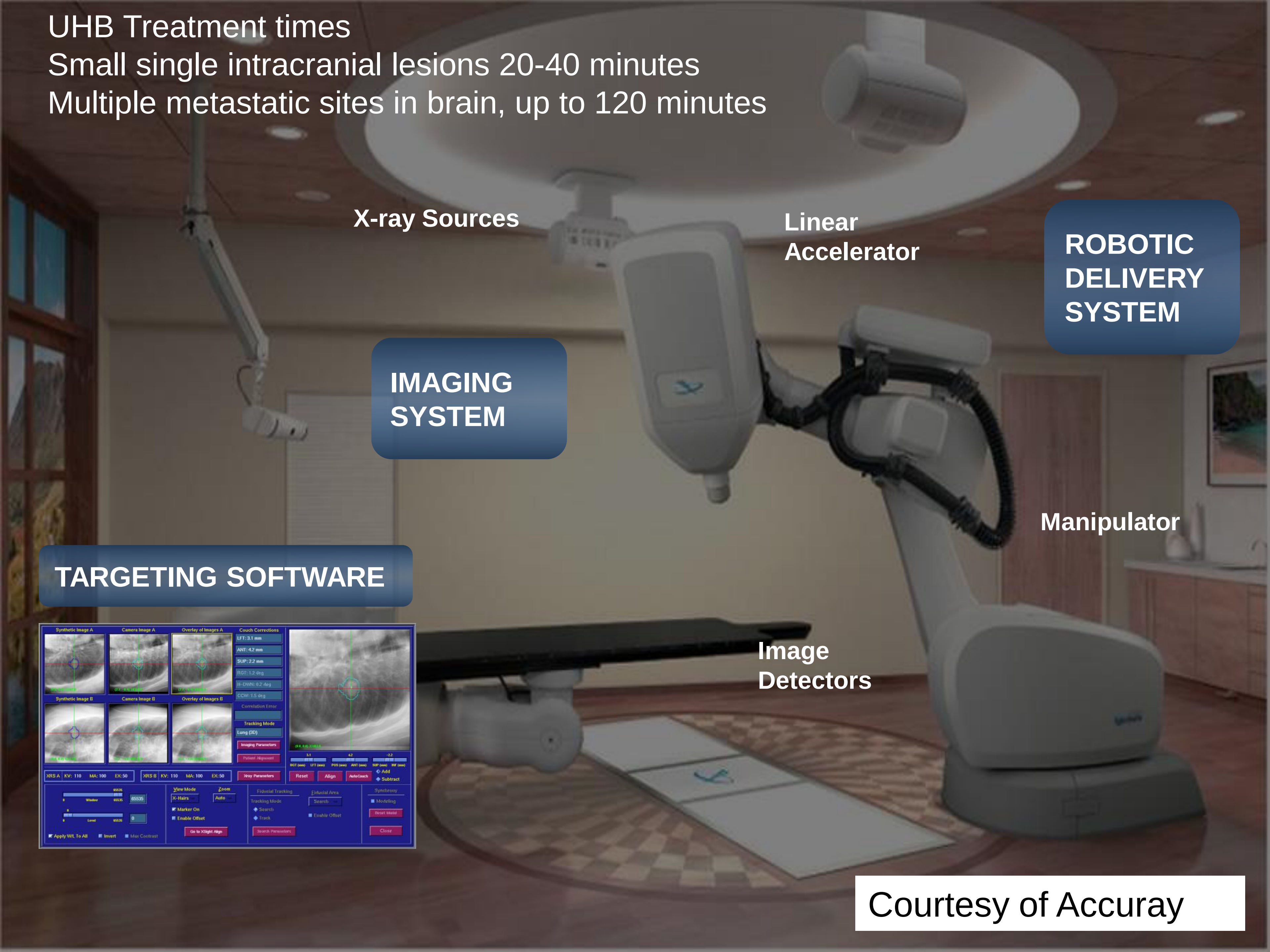
And do they still stand-up…

What is an acceptable treatment time?

- Patient comfort… less than 1hr?
- Boron kinetics…
- Is the dose being repaired?
  - Conventional wisdom
    - Low LET component repairs
    - High LET component does not
  - BNCT emerging data
    - Interaction between high and Low LET dose delivered together – low LET component repairs less (Phoenix, Birmingham PhD 2012)
    - High LET component seems to show anomalous repair in BPA-BNCT (in some cell cultures)

Dose-rate effect was observed in T98G glioma cells following BNCT. Appl Radiat Isot 2013 Dec 10. Epub 2013 Dec 10.
Yuko Kinashi, Kakuji Okumura, Yoshihisa Kubota, Erika Kitajima, Ryuichi Okayasu, Koji Ono, Sentaro Takahashi

UHB Treatment times
Small single intracranial lesions 20-40 minutes
Multiple metastatic sites in brain, up to 120 minutes



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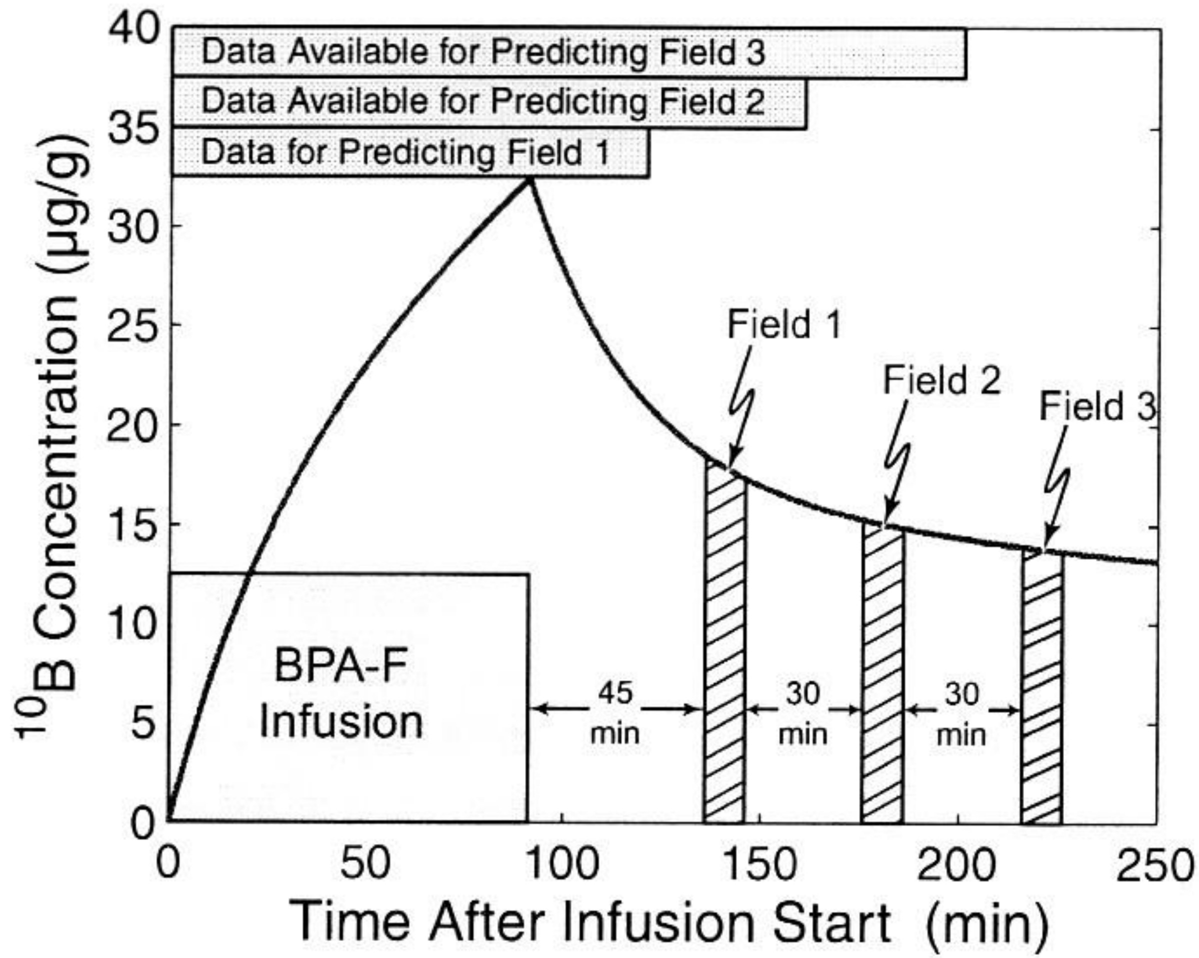
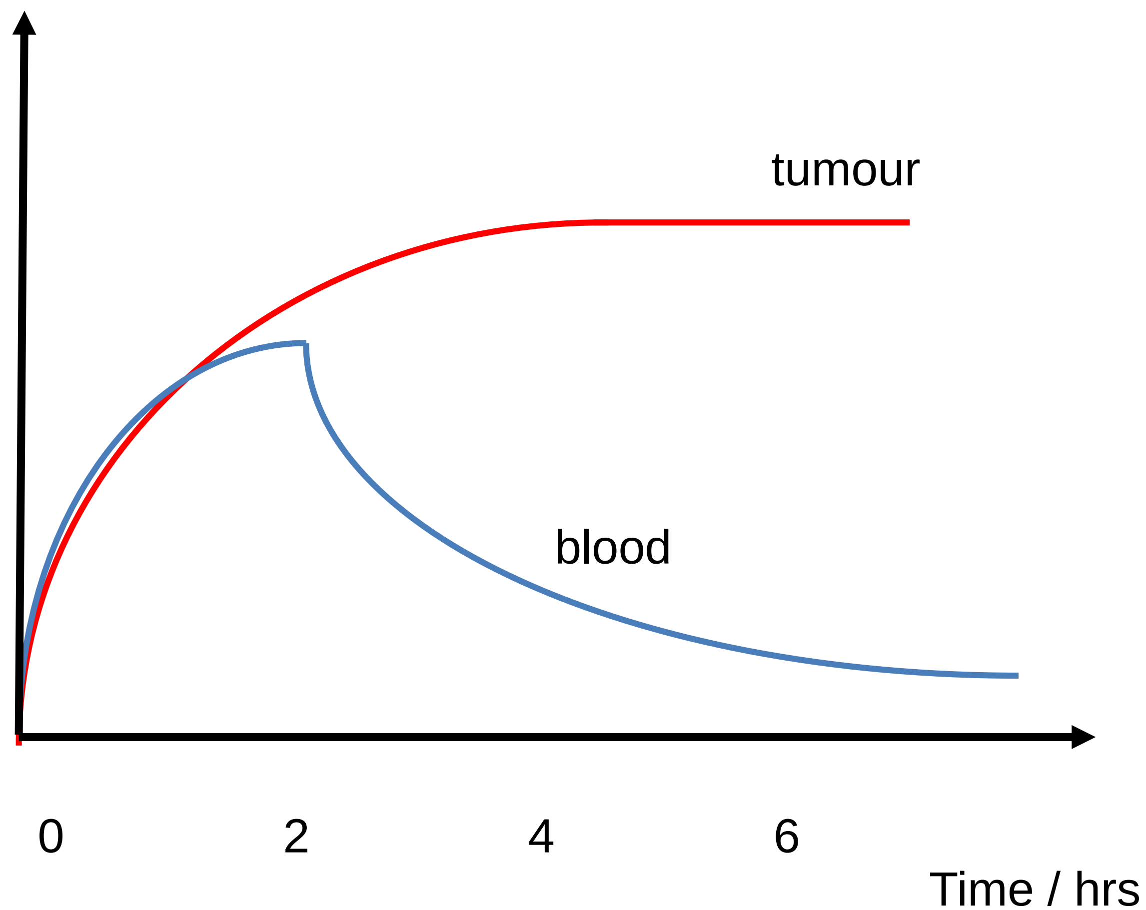
BPA pharmacokinetics



From Kiger et al, *Journal of Neuro-Oncology* **62:** 171–186, 2003.

Schematic blood and tumour boron level for BPA



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Lithium and Beryllium compared

Lithium

Higher yield at low proton energies – so source neutron spectrum is easier to downscatter to epithermal and residual fast neutron fluence is reduced

Highly malleable metal, so implanted H appears to diffuse out relatively easily

Rapidly create an large inventory of ^{7}Be (478keV photon emitter)

Poor thermal conductivity and low melting point

Lithium OK

Birmingham Accelerator beam: Estimated Treatment Times

Beam	Boron (μg/g)	Weighted Dose (Gy)*	Total time (1 field)	Approx time (2 fields)
2.8MeV Li(p,n) at 1.5mA	15	12.5	140	234
2.8MeV Li(p,n) at 1.5mA	24	12.5	110	184

*Dose is assumed to be prescribed at 3 cm deep

Lithium: Liquid or solid target?

Liquid:

- At temperatures just above melting point, vapour pressure is low
- substantial increase in heat removal capability
- substantial increase in total Li inventory
- substantial increase in technical complexity – can this be reproduced commercially?

Liquid not necessary if p-currents are 3-4mA

Lithium: thick or thin target?

Thin target:

- Substantial reduction in photon emission per neutron generated
- Main heat deposition is in the backing rather than the target
- Problems bonding to backing and blistering.

Tick target manageable with 2cm Pb shield

Lithium: to cover or not?

Covered target:

Lithium cannot sputter onto beamline

Heat deposition in thin cover can be problematic

Manage without a cover – deal with consequences

Biological weighting in BNCT

$$D_W = W_n D_n + W_\gamma D_\gamma + W_N D_N + W_B D_B$$

All neutrons regardless of energy are attributed a weighting factor of around 3 (usually 3.2, sometimes 3.0……)

Interaction between the biological effects of high- and low-LET radiation dose components in a mixed field exposure

Anna J. Mason[1], Valerio Giusti[2], Stuart Green[3], Per Munck af Rosenschöld[4,5], T. Derek Beynon[6]
& John W. Hopewell[7]

International Journal of Radiation Biology, December 2011; 87(12): 1162–1172

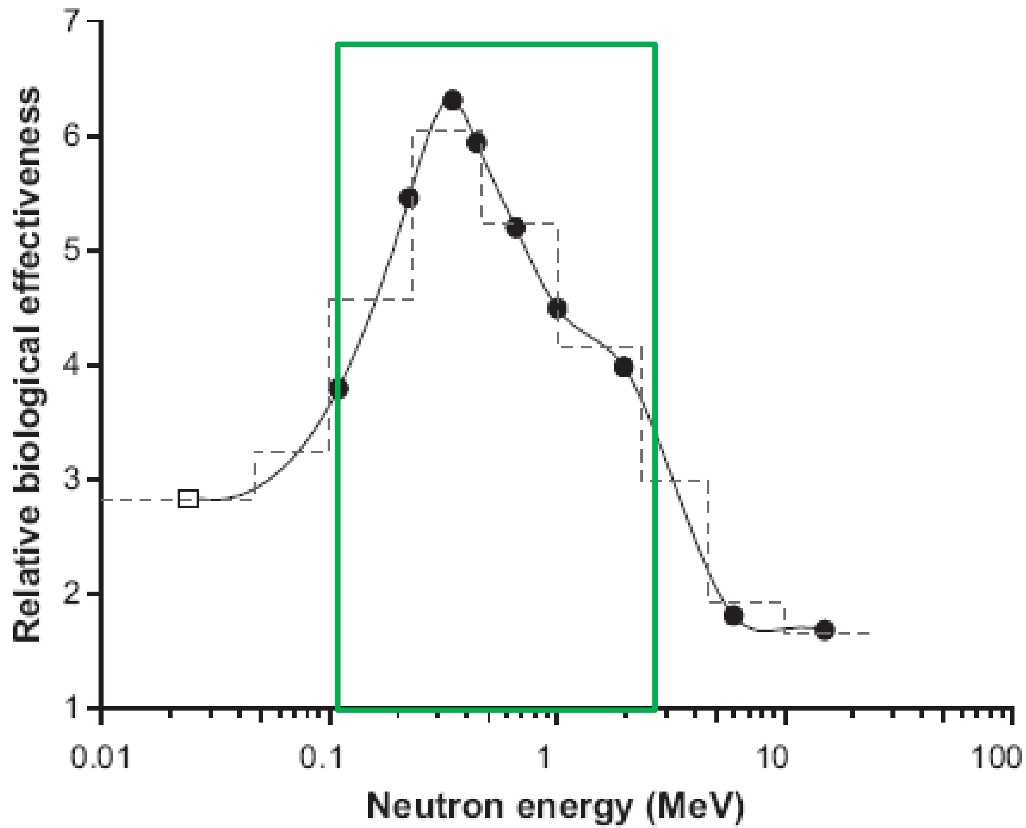
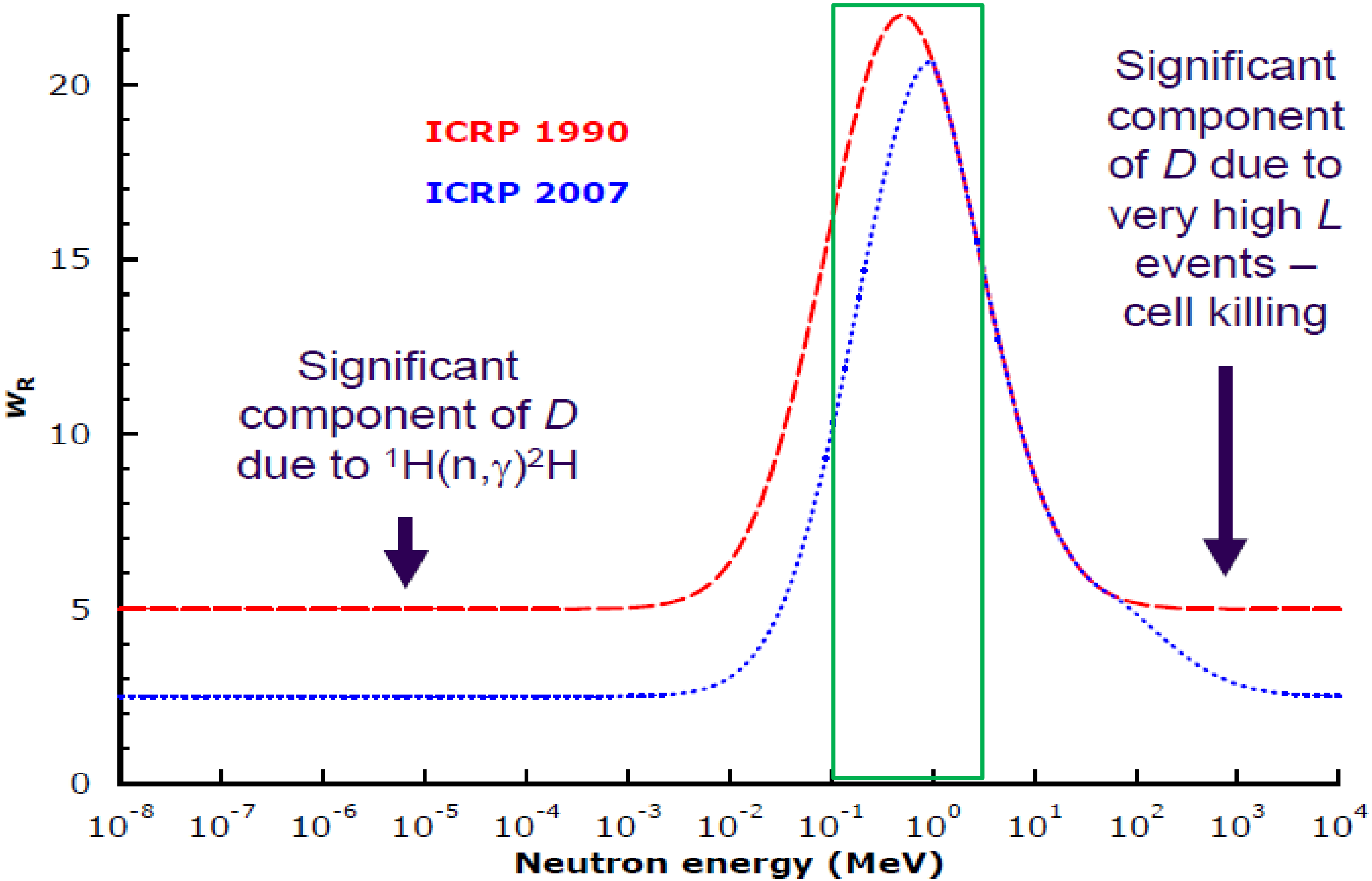
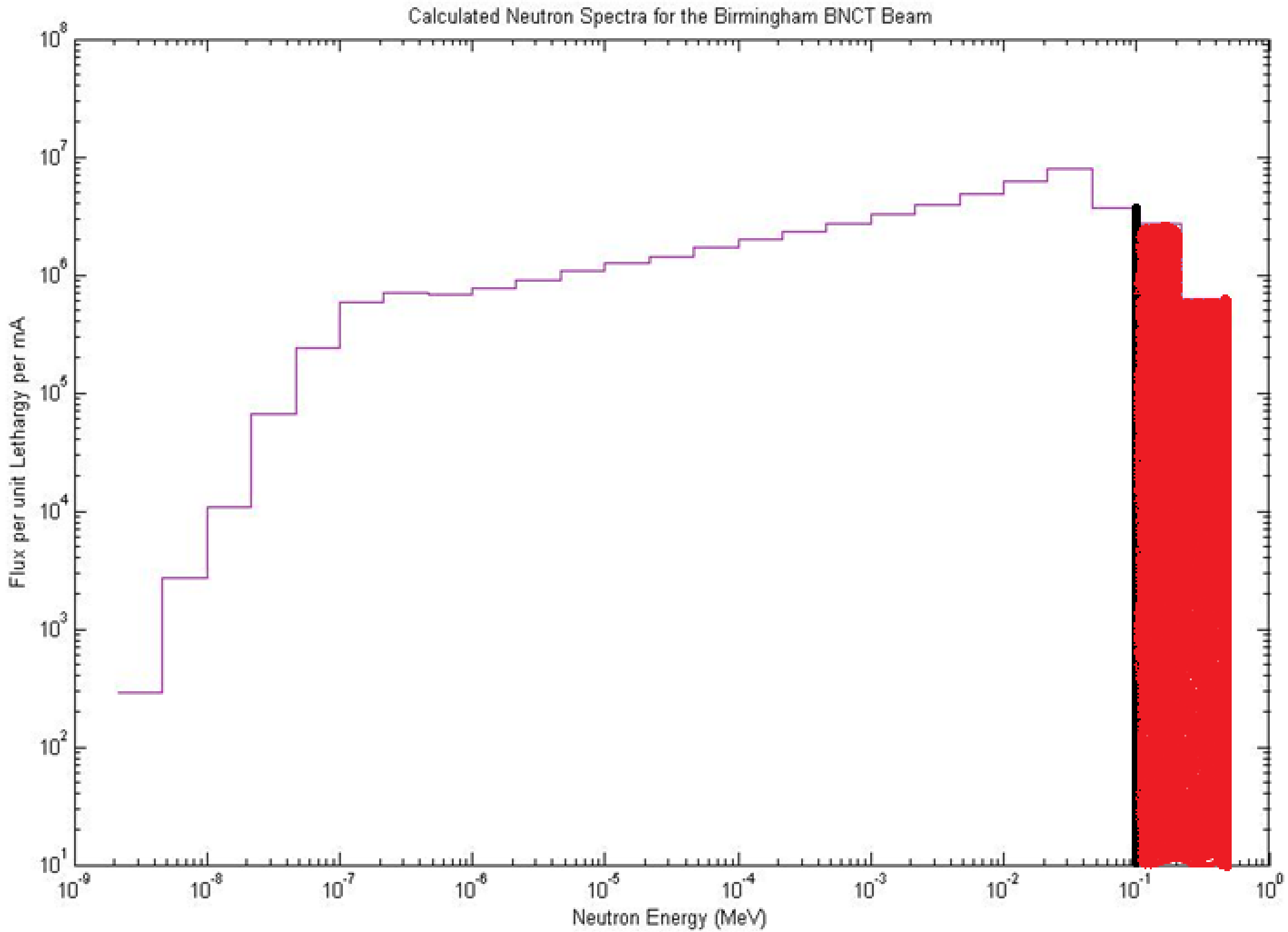


Figure 6. Variation in the RBE value of fast neutron with neutron energy, based on the common endpoint of the surviving fraction of 0.37 for V79 cells. (• data from Hall et al. 1975 and □ Morgan et al. 1988). Estimated average RBE values used in subsequent calculations for fast neutrons in different energy bands (--------).

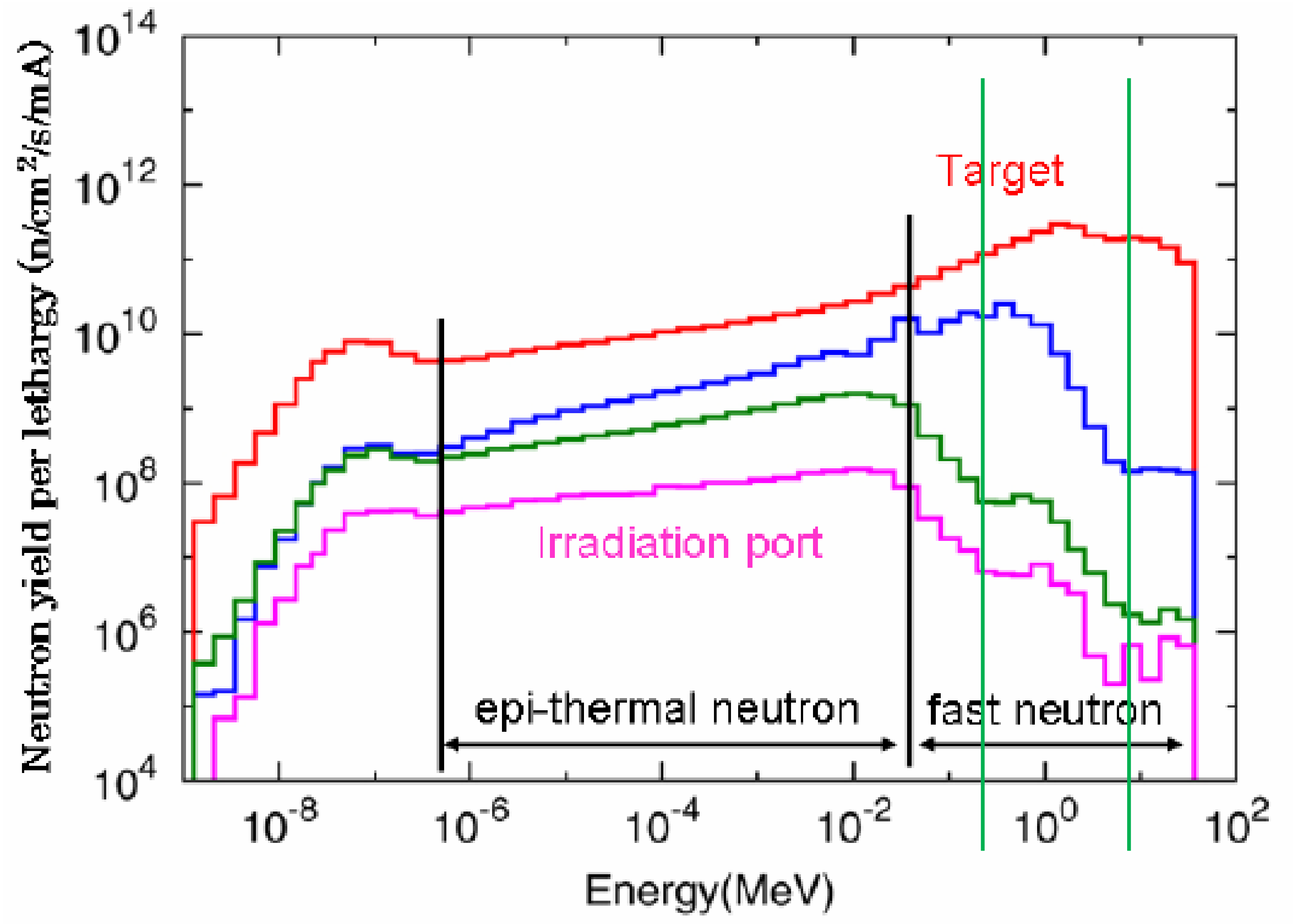
Radiation protection W_R guidance



Birmingham spectrum / unit lethargy in air



Kyoto University p(30MeV)Be system



T. Mitsumoto, K. Fujita, T. Ogasawara, H. Tsutsui, S. Yajima, A. Maruhashi, Y. Sakurai, H. Tanaka
BNCT SYSTEM USING 30 MEV H- CYCLOTRON, FRM2CCO04 Proceedings of CYCLOTRONS 2010,Lanzhou,China

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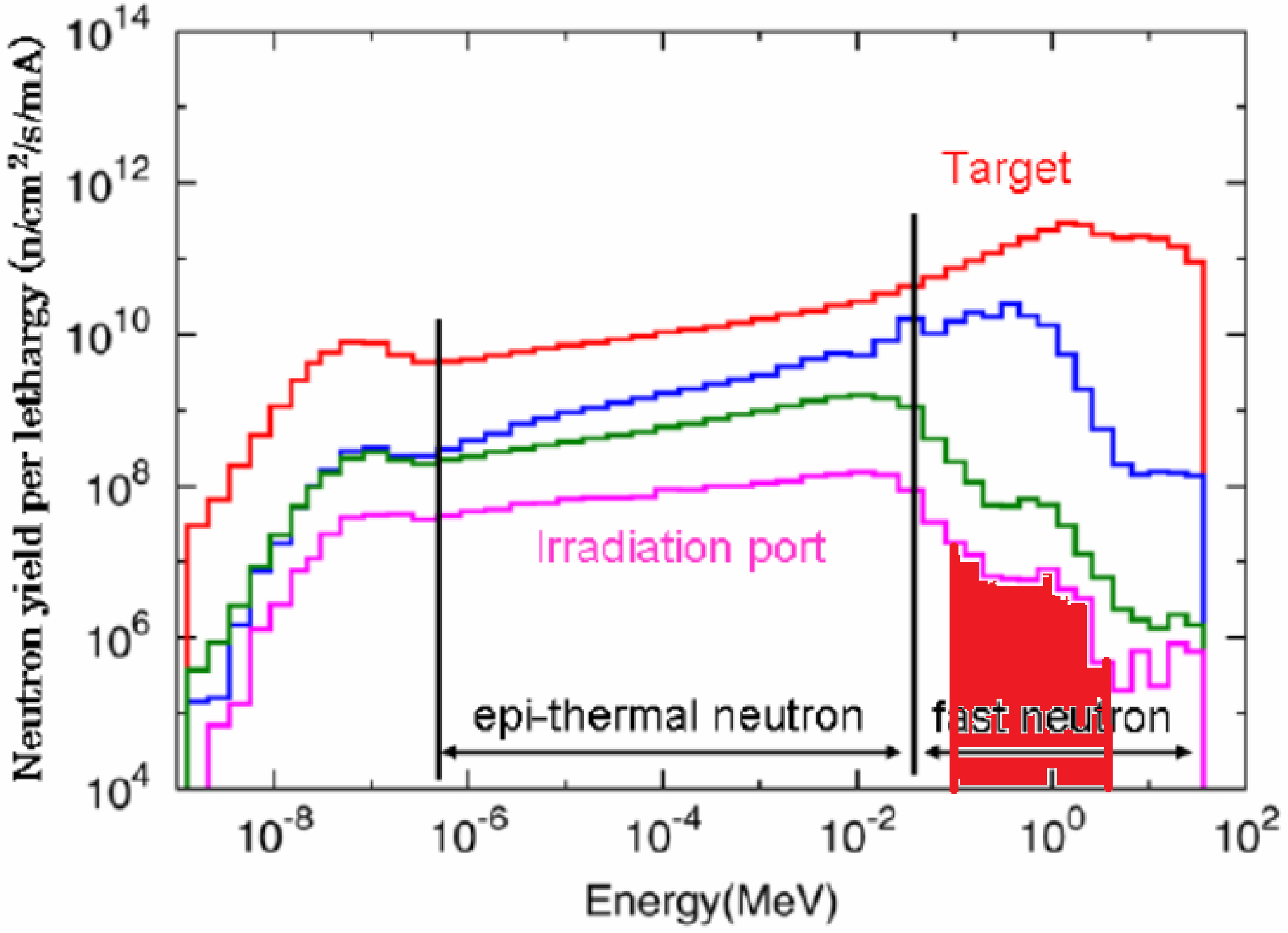
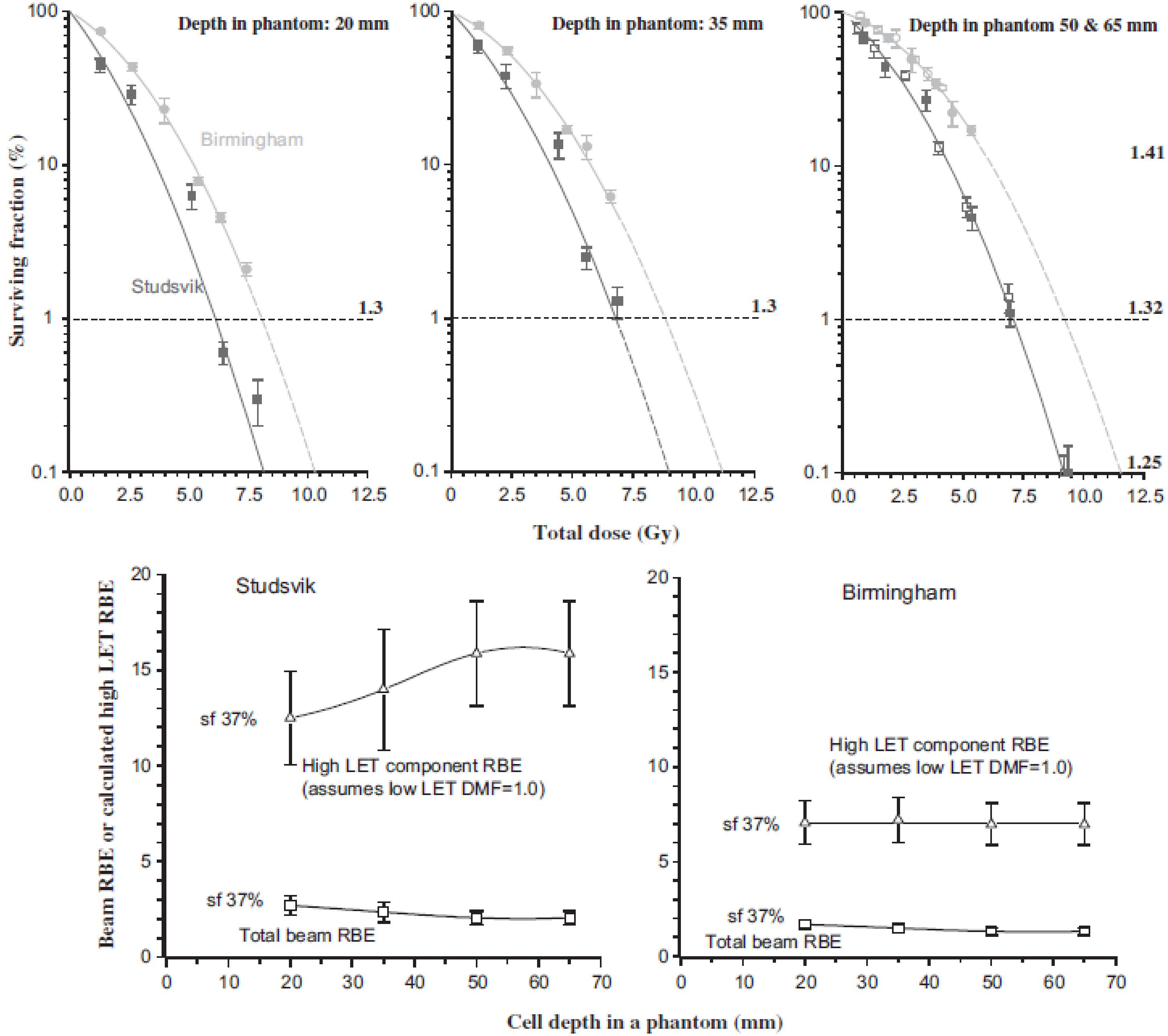


Modifield from T. Mitsumoto, K. Fujita, T. Ogasawara, H. Tsutsui, S. Yajima, A. Maruhashi, Y. Sakurai, H. Tanaka. BNCT SYSTEM USING 30 MEV H- CYCLOTRON, FRM2CCO04 Proceedings of CYCLOTRONS 2010,Lanzhou,China



From Mason et al, International Journal of Radiation Biology, December 2011; 87(12): 1162–1172

What is in the future?

- Better Boron compounds than BPA/BSH?
- (or better ways to administer BPA…)
- BPA-BNCT as a boost to XRT
- Fractionated BNCT?

All these serve to reduce the demands on the neutron beam….

What we have learned: accelerators for BNCT

- The Li(p,n) reaction is a good neutron source for generating epithermal neutrons
- The use of protons at 2.8 MeV maximises the neutron yield on our accelerator
- The extraction of a neutron beam at 90^o to the proton beam ensure fast neutron dose is minimised
- Proton currents of around 3-4 mA are sufficient for clinically manageable treatment times
- We believe this can be managed on a solid Li disk target