

**Portuguese interest in a biomedical
facility at CERN:
Radiobiology/radiophysiology studies in
loco and complemented at Coimbra
18-MeV cyclotron proton beam**

Paulo Crespo (crespo@lip.pt)



FCT

Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

on behalf of

LIP, University of Lisbon, Universidade Nova de Lisboa,
University of Coimbra, Instituto Superior Técnico, et al.

BRAINSTORMING FOR A BIOMEDICAL FACILITY AT CERN

CERN, June 25, 2012

Outline

1 Lisbon

- Universidade Nova
- LIP and University of Lisbon

2 Coimbra

- ICNAS (University of Coimbra)
- LIP and University of Coimbra

3 Animal RPC-PET

- Motivation: beyond preclinical
- Concept implementation
- Experimental results

4 Proton radiophysiology/biology

- Results in humans
- Work @ LIP/UC

5 Conclusion

1. Lisbon – Universidade Nova

Expertise in radiobiology and gene expression analysis:



CIGMH

Department of Genetics
Faculty of Medical Sciences
Universidade Nova de Lisboa

Expertise and Know-how

Experience: Radiation biology, genotoxicology of radiation, Boron neutron capture

- **Cytogenetic assays** Chromosomal aberrations
Micronuclei
- **Cell viability assays** MTS, MTT, clonogenic assays
- **Gene expression analysis** Real time QPCR
- **Apoptosis assays** Spectrofluorimetry, Fluorescence microscopy
- **γ H2AX assay** Fluorescence microscopy

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1. Lisbon – LIP and Universidade de Lisboa

Expertise in Monte Carlo, dosimetry, and radioprotection:

LIP-Lisbon Expertise fields

Plastic scintillators

Low energy dosimetry/ radioprotection and shielding

Fluka and GEANT4 simulation

Alpha particle dosimetry

Fast MC for alpha particle transport

Scan path optimization for active beam delivery in charged particle therapy.

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2. Coimbra – ICNAS: hosts 18-MeV proton cyclotron from University of Coimbra

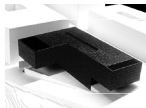
Expertise in cyclotron physics, radiobiology, & radiophysiology:

INSTITUTO DE CIÊNCIAS NUCLEARES APLICADAS À SAÚDE



ICNAS Expertise

- Cyclotron (18MeV proton / 9MeV deuteron) with beam extraction port
- Full GMP radiochemistry lab (11C, 18F, etc)
- Cell and tissue culture (CO₂ incubator, LAF workstation, etc)
- Simple animal model: C. Elegans (we use for radiobiology studies)
- Complex animal models (rats and mice):
 - Tumor models (xenografts) for osteosarcoma, breast, etc
 - short (1-3 days) studies can be done.
 - Areas for longer (longitudinal) studies are being implemented
- Animal imaging:
 - MicroPET, CT, XR, optical (bioluminescence and fluorescence)
 - 9.4 T animal MRI being implemented



ICNAS

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2. Coimbra – LIP and University of Coimbra

Expertise in human and small animal nuclear imaging
(Monte Carlo, detector construction, image reconstruction):

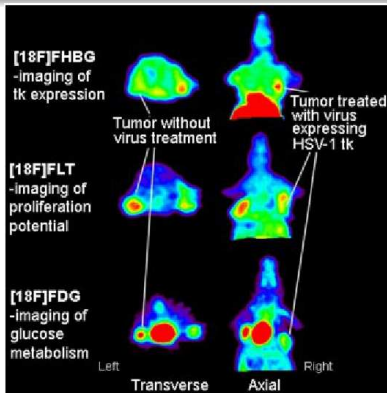
- Human, whole-body, single-bed resistive plate chamber PET (RPC-PET) with demonstrated coincidence time resolution of 300 ps FWHM: **for diagnostic, under construction**
- Small-animal RPC-PET with demonstrated submillimetric spatial resolution (slides 7-9): **for radiopharmacy and e.g. particle radiophysiology, under final construction**
- Real-time treatment dose verification (RTmon) for external X-ray beam radiotherapy with (1) demonstrated submillimetric positioning accuracy, and (2) unprecedented correlation with dose effectively delivered: **for assisting X-ray-beam therapy, small prototype under construction**



3. Animal RPC-PET (aRPCPET)

Motivation: the demonstrated submillimetric resolution of aRPCPET (slide 9) potentiates preclinical studies beyond those offered today

- aPET is supported mainly by pharmaceutical and fundamental biomedical research, but: **particle therapy may also profit strongly** (as it already does).



- From **Athinoula Martinos Center for Biomedical Imaging**
- FHBG = fluoro-hydroxy-metil-butyl-guanina.
- HSV-1 = Herpes simplex virus-1.
- FDG = fluoro-desoxy-glucose.
- FLT = desoxy-fluorotimidina.

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3. Animal RPC-PET

Concept (under final implementation)

- Innovative animal RPC-PET system proposed at LIP (E.g. Blanco et al. TNS 2006).

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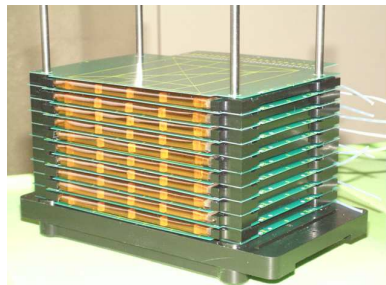
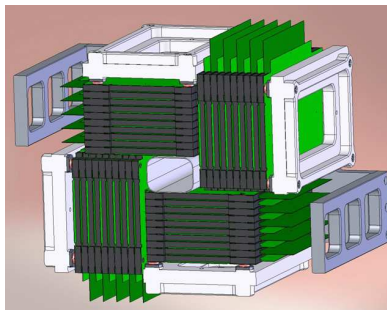
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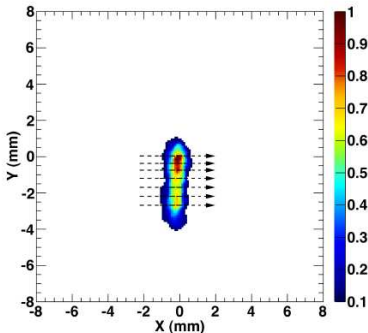
Full head, now being commissioned

3. Animal RPC-PET

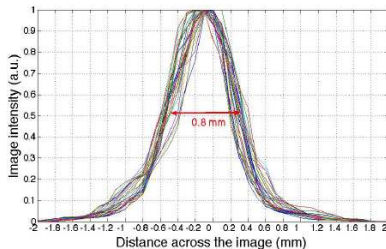
Submillimetric (not-yet-optimized) experimental results:

- E.g. radioactive source was made in house, is nonuniform, and has a suboptimal, cylindrical-like disk shape (Martins et al. 2012 IEEE MIC submitted).

Axial view



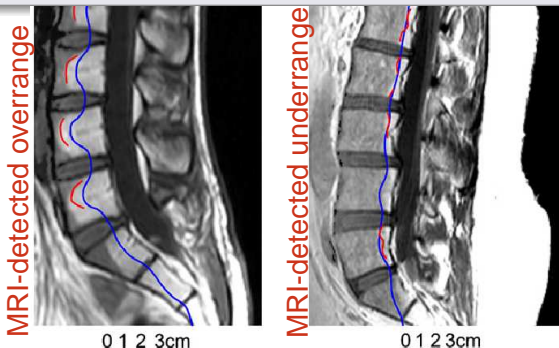
Line profiles across
axial view: FWHM < 1 mm



4. Proton radiophysiology/biology

Medulloblastoma: range deviations by T1-weighted MRI

- Observation: (1) fatty conversion in the vertebral bone marrow; and (2) edema in the posterior part of the vertebral bodies (**Stevens et al AJR 1990**).
- Unknowns: (1) higher RBE at end of proton range?
(2) Bone marrow edema and vascular congestion?
(3) Other? → **Radiophysiology @ CERN/Coimbra**



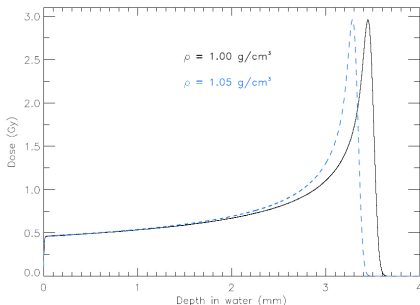
From Gensheimer et al
IJROBP 2010

4. Proton radiophysiology/biology

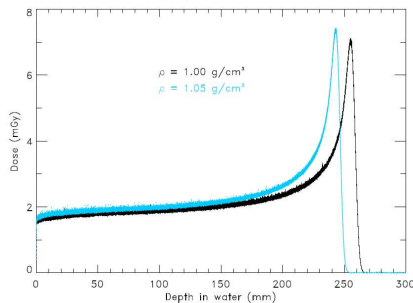
Ongoing work at LIP/University of Coimbra (ICNAS)

- Design and construction of a proton irradiation setup for proton radiobiology/radiophysiology (et al.) (Ghithan PhD ongoing).
- Useful for particle RT community, especially if results may be crosschecked elsewhere (LEIR@CERN?)

18 MeV, $\Delta R = 163 \mu\text{m}$



200 MeV, $\Delta R = 1.2 \text{ cm}$



Cunha MSc thesis 2010

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4. Proton radiophysiology/biology

Ongoing work at LIP/University of Coimbra (ICNAS)

- Design and construction of a proton irradiation setup for proton radiobiology/radiophysiology (et al.)
([Ghithan et al 2012 IEEE NSS submitted](#)).
- Monte Carlo (Geant4) code development ([Pinto MSc thesis 2010](#), [Ghithan PhD ongoing](#)) and validation
([Ghithan PhD ongoing](#))

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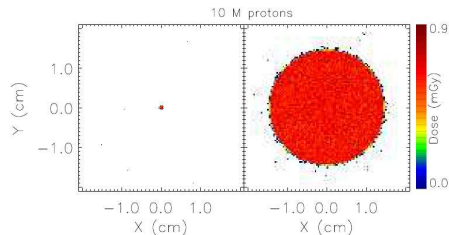
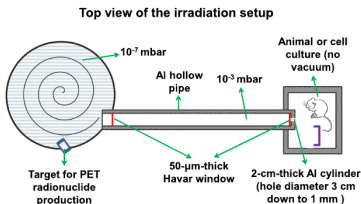
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5. Conclusions

Biomedical facility at LEIR@CERN

- Highly-desired by countries without a particle therapy center and willing to contribute to particle radiobiology/radiophysiology studies, as demonstrated with several examples throughout this talk
- The scientific and technological outputs of these studies are in turn highly-desired by the particle therapy community for improving pertinent radiobiological/radiophysiological knowledge, models, and most importantly clinical outcomes
- Biomedical facility at LEIR@CERN seems to be a **win-win** scenario for all parties involved

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Thank you for your attention