Feasibility of using ^{18}O-enriched phantoms for PET range verification of proton therapy treatment planning

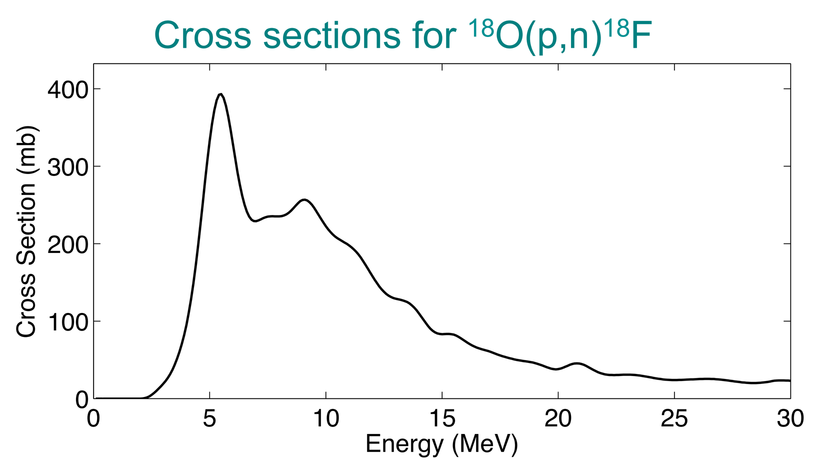
Center for Advanced Medical Imaging Sciences

K. Grogg[1], X. Zhu[1], J. Chang[2], B. Winey[3], J.A. Correia[1], G. El Fakhri[1]

[1] Dept. of Radiology, Mass General Hospital; Harvard Medical School Boston, MA, USA
[2] Florida Radiation Oncology Group, Jacksonville, FL, USA
[3] Dept. of Radiation Oncology, Mass General Hospital, Boston, MA, USA

Introduction

- Proton beam therapy offers a conformal dose due to Bragg peak, but introduces sensitivity to beam range [1]
- PET scans present the possibility of verifying dose delivery location
  - PET isotopes are produced by nuclear interactions while the dose is mainly from electromagnetic interactions
  - Typical *in vivo* PET production does not give dose like distributions [2]
- PET images of ^{18}F produced from the reaction ^{18}O(p,n)^{18}F have a dose-like distal falloff due to the high cross section at low energies



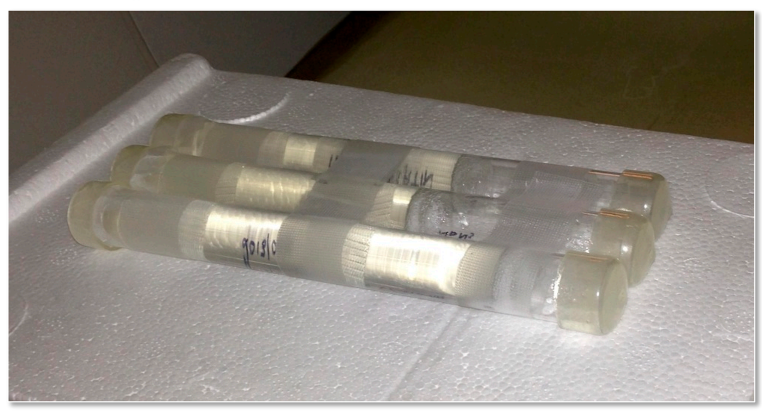
Cross section by proton energy for the reaction ^{18}O(p,n)^{18}F. Cross sections above 30 MeV were extrapolated

Objectives

- Explore the feasibility of using ^{18}O based phantoms for quality control in proton therapy
  - Would make 3D range verification possible using a direct comparison between planned range and PET activity

Methods

- PET scans were taken of a multi-part water + gelatin phantom, after irradiation with proton beam
  - Phantom consisted of three tubes with different mixtures: 100% $H_2{}^{16}O$ and 0% $H_2{}^{18}O$, 50% $H_2{}^{16}O$ and 50% $H_2{}^{18}O$, and 20% $H_2{}^{16}O$ and 80% $H_2{}^{18}O$
  - Irradiated with a uniform field of 48 Gy, range 10 cm and modulation of 6 cm



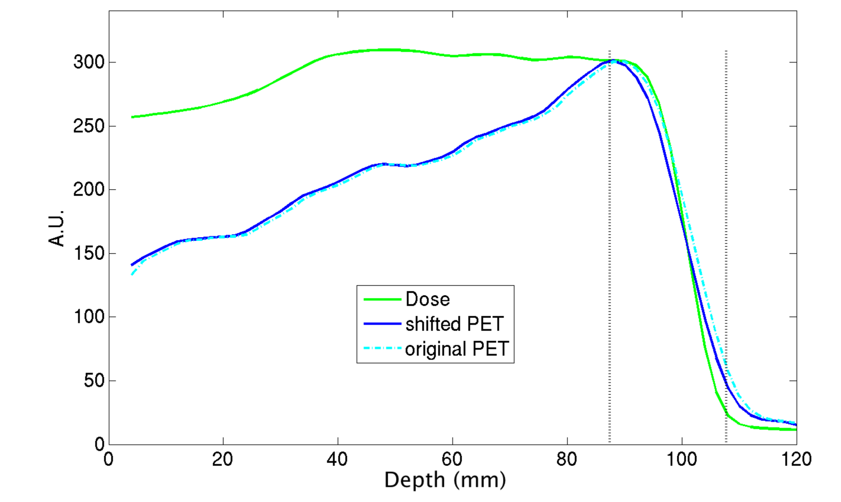
- A 4 hour PET scan was taken 30 minutes after irradiation, and reconstructed for both the first 15 minutes and last 2 hours
  - Initial 15 minutes of the scan was dominated by ^{11}C activity ($t_{1/2}$ = 20 min.) from the reaction ^{16}O(p,3p3n)^{11}C
  - Last two hours were dominated by ^{18}F activity ($t_{1/2}$ = 109 min.)
- A Geant4 based Monte Carlo program [4] was used to simulate the planned delivery of the proton beam and interaction with the ^{18}O water phantom
  - Each tube was specified with the appropriate density and elemental composition based on the percent of ^{18}O present
  - The production of ^{18}F was calculated with the cross sections shown in the figure to the left [5]

Interaction	Threshold (MeV)	Half-life (min)
^{16}O(p,pn)^{15}O	16.79	2.037
^{16}O(p,2p2n)^{13}N	5.66	9.965
^{14}N(p,pn)^{13}N	11.44	9.965
^{12}C(p,pn)^{11}C	20.61	20.39
^{14}N(p,2p2n)^{11}C	3.22	20.39
^{16}O(p,3p3n)^{11}C	27.5	20.39
^{18}O(p,n)^{18}F	**2.6**	**109.77**

Table of the nuclear interaction production of PET isotopes and their half lives

Note that the ^{18}O(p,n)^{18}F threshold of 2.6 MeV is lower than the other thresholds, and the longer half life makes it easy to distinguish from other isotopes

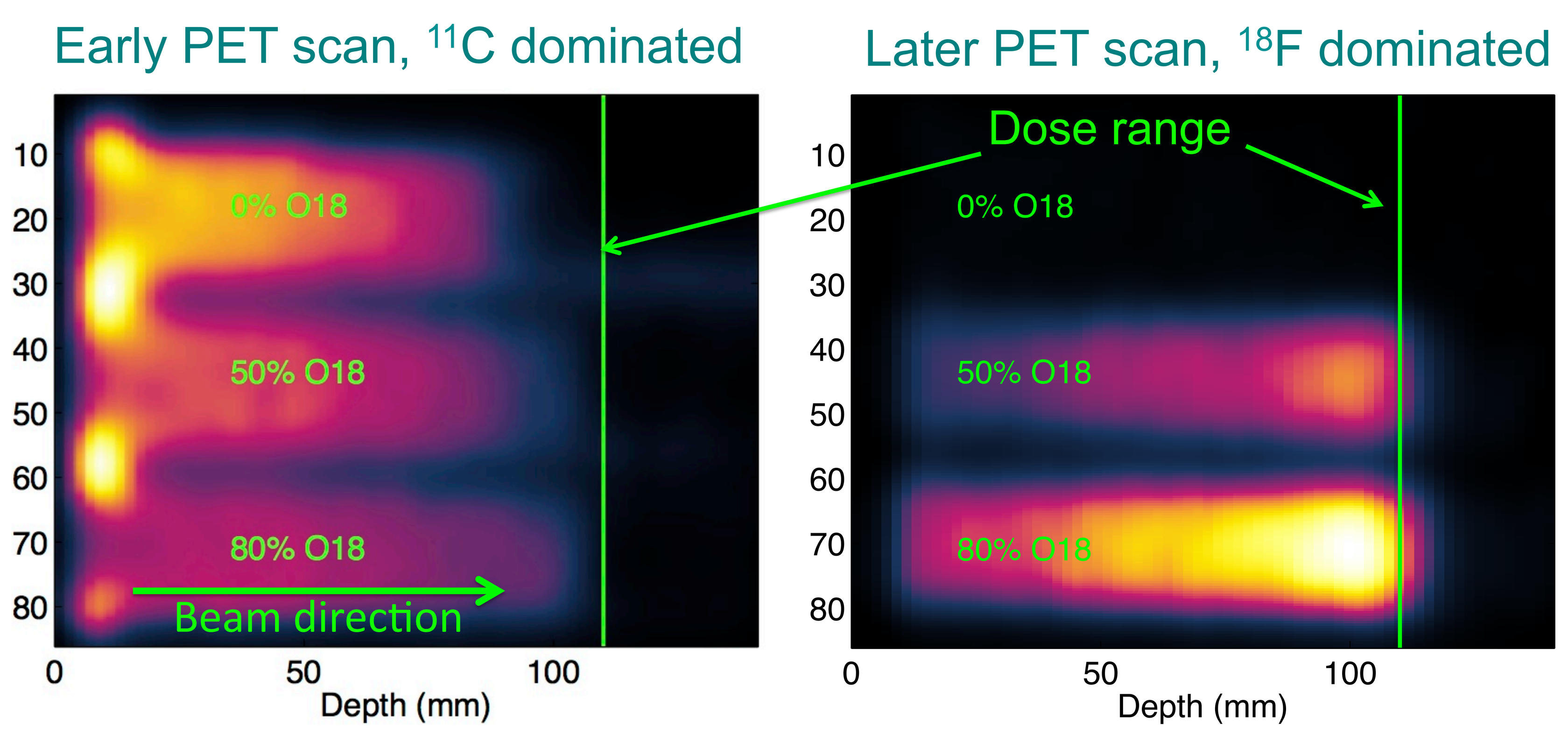
- Analysis of range
  - Profiles along the beam path for the dose and activity concentration for each of the tubes were averaged within the center of tubes
  - The ranges for the ^{18}O distributions were then compared using the “shift method” [3] as follows:
    - The two distributions were first normalized by their distal peaks
    - A falloff comparison window was established between the distal peak of the dose, and the depth where PET dropped to 20% of the maximum
    - Falloffs of the dose and the PET were compared as one distribution was shifted in depth in steps of 0.1 mm until the residual sum of squares was minimized



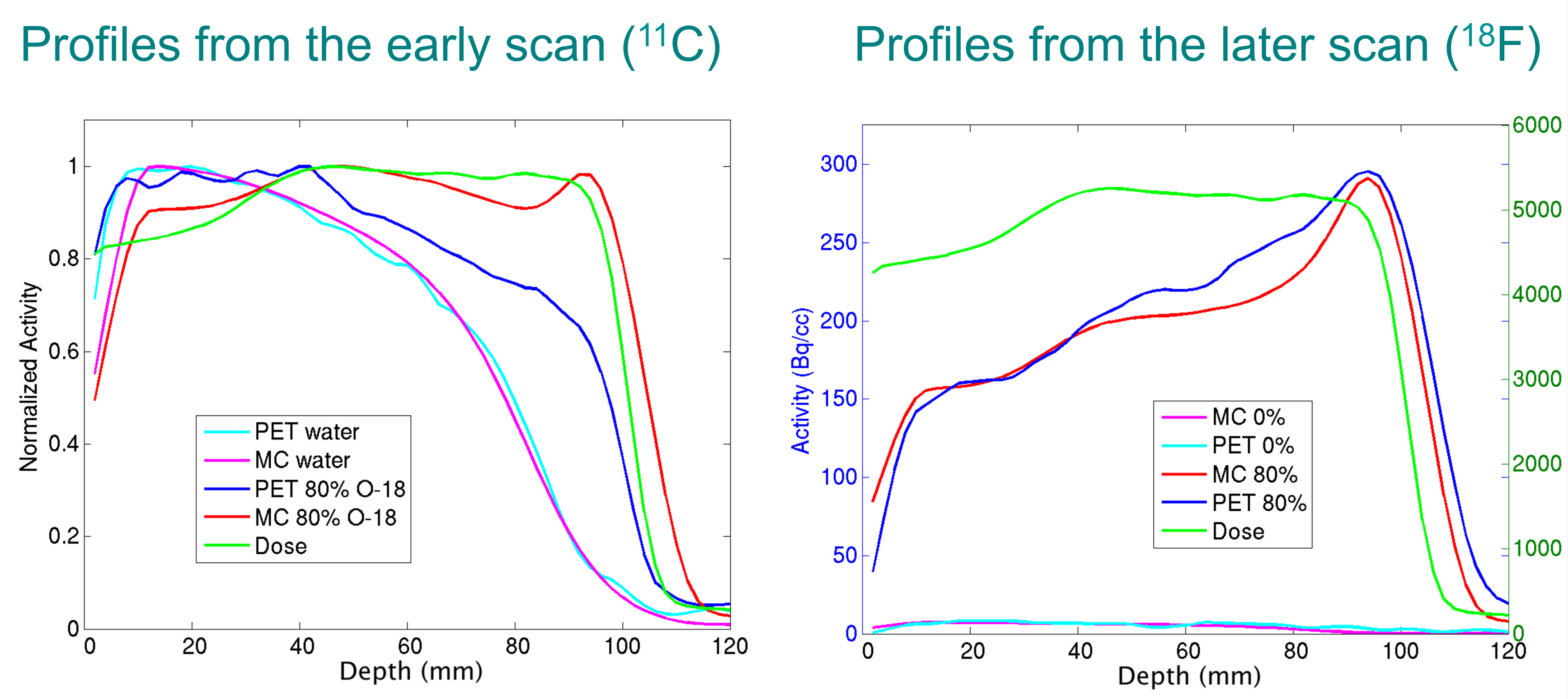
Profiles of the dose, original PET distribution, and the PET distribution after shifting it -0.5 mm to the minimum RSS

Results

- The range of the ^{18}F activity induced from proton irradiation of ^{18}O water coincides better with the dose than the ^{11}C activity
  - For the tubes containing some percentage of ^{18}O, the distal falloff of the dose and ^{18}F PET signal agreed within 2.0 ± 0.5 mm (2.0%)
- In the latter scan, the high activity level at the end of the proton range, where proton energy is low, shows the effect of the high cross section at low proton energies for ^{18}O(p,n)^{18}F



PET distributions in the irradiated ^{18}O phantom for the first 15 minutes of acquisition (left) and last two hours (right). Dose range (50% of maximum) is indicated with a vertical green line. The ^{18}F signal, unlike the ^{11}C signal, coincides with the dose depth.



Profiles of the PET activity along the beam path shown with the corresponding MC-PET and MC-dose (green) profiles, for regular water and 80% ^{18}O water. The left profiles are normalized to emphasize shape.

Conclusions

- We have successfully used an ^{18}O enriched water phantom to image the depth of the proton dose range from a planned delivery
- These ^{18}O phantoms will provide direct evidence of the robustness of the treatment planning and serve as a cross check for patient treatment verification methods
- It can also be used to compare the effectiveness of different delivery methods, such as passive beam scanning versus spot beam scanning
- Future work is planned to test the ideal concentration of ^{18}O for use with early and late scans, to be able to compare typical in-room *in vivo* like results [6] with the dose-like ^{18}O falloff

References

1. H. Paganetti, “Range uncertainties in proton therapy and the role of Monte Carlo simulations,” *Phys. Med. Biol.*, vol. 57, pp. R99-R117, 2012.
2. K. Parodi, H. Paganetti, H.A. Shih, “Patient study of in vivo verification of beam delivery and range, using positron emission tomography and computed tomography imaging after proton therapy,” *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 68, pp. 920-34, 2007.
3. A. Knopf, K. Parodi, H. Paganetti, E. Cascio, A. Bonab, and T. Bortfeld “Quantitative Assessment of the physical potential of proton beam range verification with PET/CT,” *Phys. Med. Biol.* vol 53, pp. 4137-4151, 2008.
4. H. Paganetti, K.P. H. Jiang, K. Parodi, R. Slopsema and M. Engelsman, “Clinical implementation of full Monte Carlo dose calculation in proton beam therapy,” *Phys. Med. Biol.*, vol. 53, pp. 4825-4853, 2008.
5. E. Hess, S. Takács, B. Scholten, F. Tárkányi, H. H. Coenen and S. M. Qaim Excitation function of the ^{18}O(p,n)^{18}F nuclear reaction from threshold up to 30 MeV. *Radiochim. Acta* 89, pp. 357-362, 2001.
6. X. Zhu, S. Espana, J. Daartz et al. “Monitoring proton radiation therapy with in-room PET imaging,” *Phys. Med. Biol.*, vol. 56, pp. 4041-4057, 2011.

Work funded by NIH grants R21CA153455, R21EB12823 and T32RB013180