F-18 FMISO PET Imaging in Cancer: Clinical Experience:

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Issues in Evaluating Hypoxia

The Ideal Method

- Heterogeneous nature of hypoxia
- “Snapshot fashion”
- Temporal changes
  - Repeat measurements
- Reproducibility
- Invasiveness
- Accessibility
  - Tumor location

FMISO PET - Coronal
**[F-18] FMISO PET Imaging**

- Fluoromisonidazole is retained in hypoxic tissue
- Partition Coefficient $\sim$ 1, same value as antipyrine
  - early image is BF, late image is PC
- Normoxic tissue T:B $\sim$ 1 (narrow range)
- T:B $\geq$ 1.2 indicates hypoxia
- Hypoxic volume (HV)

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Chemical reactions:

$\text{H}_2\text{O}_2 \xrightarrow{\text{OH}^-} \text{O}_2^- \xrightarrow{\text{R-NO}_2} \text{R-No}^-$

$\text{O}_2^- \xrightarrow{\text{O}_2} \text{R-NO}_2\text{O}^-$

$\text{R-NO}_2\text{O}^- \xrightarrow{4\text{e}^-} \text{R-N=O} + \text{R-NH}_2$

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Graph:

- **Frequency (pixels)**
- **Tumor**
- **Brain**

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Example FMISO PET Images

Coronal FDG

Coronal FMISO
FMISO Patient Studies

– Total Number - studies : 390
– Total Number - patients: 291
– Head & Neck : 110
– Brain : 48
– Lung : 36
– Sarcoma : 40
– Breast : 20
– Cervix : 20
– Others : 17

Head/Neck cancer

Breast cancer
Heterogeneity in Hypoxia

Head and Neck Cancer

FDG

Max. SUV = 8.5

FMISO

Max T:B = 1.5 (6.5 mL)
Right Max = 1.4 (1.5mL)
Left Max = 1.1

Intratumoral Heterogeneity
FMISO vs Electrodes

Liposarcoma

Electrode measurements

FMISO Coronal PET

FMISO uptake

Osteosarcoma

Electrode measurements

FMISO Coronal PET

FMISO uptake

Mean = 13.1
Median = 7.15
% below 2.5 = 0%
% below 5 = 26.2%
n=42

Mean = 30.3
Median = 32.9
% below 2.5 = 14%
% below 5 = 23%
n=77

Vesselle HJ & Rajendran JG
Single Tracer Approach?
Hypoxia vs Glucose Metabolism

Rajendran JG et al Clin Can Res 10; , 2004
Information on Hypoxia?

Tumor Hypoxia

Pre-therapy
- Characterizing tumor
- Prognostication
- Choice of therapy
  - Local
  - Systemic

Intra-therapy
- XRT Boost
- Hypoxic cell cytotoxins
  - Tirapazamine
- Therapy modification
Pre-Therapy Hypoxia in Head and Neck Cancer
Response To Treatment

FMISO: $p = 0.05$

FDG: $p = 0.1$

Rajendran JG et al. 2004
Pre-Therapy Hypoxia in Head and Neck Cancer

Overall Survival


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Pre-therapy Hypoxia and Recurrence

Characteristic FMISO Curve Types

Type 1 (washout; no disease recurrence)

Type 3 (accumulation; recurrence in 5/6 patients)

FMISO in Glioblastoma


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FMISO in Cervical Cancer Survival

Rajendran JG et al. AACR Mtg 2007
F-MISO And Patient Selection for TPZ


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Evaluating Re-oxygenation with F-18 FMISO PET

- FMISO is able to image hypoxia in primary tumor and metastatic nodes
- Persistent hypoxia after therapy (in 33%) is a target for boost radiation
- Intra-therapy hypoxic sub-volume to be used for the boost
Sequential FMISO Imaging: Change in Hypoxic Volume

Pre-therapy
- FDG 5/11/04
  - Primary SUV 9.4
- FMISO 5/12/04
  - Primary T:B = 1.45
  - Primary HV = 5.6

4 weeks therapy
- FMISO 6/10/04
  - Primary T:B = 1.22
  - Primary HV = 0.2

Rajendran JG et al., 2004

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Sequential FMISO Imaging:
Change in Hypoxic Volume

49 yo F with Rt frontal GBM resected 9/19/01
MRI, FDG, FMISO pre therapy
Treated with 15 Gy neutrons, 3 / wk
Post neutron image shows no reoxygenation

The thermometer is B/W in the normal range (<1.2) and changes to color above the hypoxia threshold of 1.2.

Spence AM, Univ of Washington
Radiation Therapy Plan Based on FMISO PET Hypoxia Boost

FMISO PET: Tumor:Blood vs Parametric Imaging

FMISO Flux = $K_1 k_3 / (k_2 + k_3)$

Rajendran JG, Narayanan M et al, ASTRO, 2006

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FMISO studies at UW were supported by NIH grants P01 CA42045 and Seattle Cancer Consortium Pilot grant.
Thank You