Applications in Medicine
Past and Future

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UW-Madison
Societal Impact: Medical Imaging
Digital Subtraction Angiography

Kidney transplant and a stent placement.

Charles Mistretta
Prof of Medical Physics
Societal Impact: Medical Imaging
Osteoporosis and bone mineral densitometry
Societal Impact: Medical Imaging
MRI Flow Contrast Angiography
Molecular imaging in oncology – targeting hallmarks of cancer

Hanahan, Cell, 100, (2000), 57
Initial protocol idea

Initial Protocol Assessment Team (IPAT)
Radiologists, Physicists, Oncologists

Imaging Protocol Advisory and Review Teams (IPARTs)
Radiologist, Physicist, Statistician

CT  MR  PET  US

Clinical Imaging Shared Facility (CISF)
Research Program Managers, Research Technologists, IPART

Image Analysis Center (IMAC)
Imaging Scientists, IPART

Design of imaging procedures

Implementation of imaging procedures

Analysis of imaging data
Acute myeloid leukemia (AML)

- **Standard treatment of AML**: induction chemotherapy for 7 days, bone marrow aspirate and biopsy at 2 wks, repeat chemotherapy if needed

- The results of the bone marrow biopsy are often difficult to interpret and the predictive power is poor

- Use imaging as a predictive biomarker to segregate patients into high and low risk groups
FLT PET response

Complete Responder

Resistant Disease

Pre-treatment

Post-treatment

Chemo

Chemo

SUV

10

5

0
Timing of the scan does not matter

<table>
<thead>
<tr>
<th></th>
<th>SUV$_{\text{mean}}$</th>
<th>SUV$_{\text{max}}$</th>
<th>Coef. Of Var</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Remission (aplastic, day 14)</td>
<td>0.81 ± 0.03</td>
<td>3.6 ± 0.4</td>
<td>0.33 ± 0.02</td>
</tr>
<tr>
<td>Resistant Disease (post-therapy, day 2)</td>
<td>1.60 ± 0.14</td>
<td>11.4 ± 0.8</td>
<td>0.71 ± 0.04</td>
</tr>
</tbody>
</table>

$p < 0.001$
Personalization of therapy

FDG

FLT

CuATSM

What to dose paint?
Personalization of therapy

When to dose paint?

Pre-treatment

Mid-treatment
(1 wk of XRT)

FLT-PET/CT
Societal Impact: Medical Imaging
Tomotherapy

Photos: http://www.psl.wisc.edu/projects/large/tomo
Microscopic Energy Deposition

Low-LET tracks in cell nucleus
e.g. from γ-rays

A dose of 1 Gy corresponds to ~1000 tracks

High-LET tracks in cell nucleus
e.g., α particles

A dose of 1 Gy corresponds to ~4 tracks

-1 μm
Direct Damage to DNA

- 10 keV electron (13.4 nm spacing)
- 1 MeV proton or 30 MeV alpha particle
- 80 keV proton or 5 MeV alpha particle
- 0.7 MeV alpha particle or 50 MeV carbon-12 ion
- 5 MeV carbon-12 ion

Scale: 2 nm
It must have occurred to many people that the particles themselves now become of considerable therapeutic interest.

... specific ionization or dose is many times less where the proton enters the tissue than it is in the last centimeter ...

These properties make it possible to irradiate intensely a strictly localized region...

Thus the biological effects near the end of the range will be considerably enhanced due to greater specific ionization...

It will be possible to treat a volume as small as 1 c.c. anywhere in the body and to give that volume several times the dose of any neighboring tissue.

In treating large volumes ... accomplished by interposing a rotating wheel of variable thickness, corresponding to the tumor thickness, between the source and patient.

Heavier nuclei, such as very energetic carbon atoms, may eventually become therapeutically practical.
Depth dose distribution of various radiation modalities

- 254 MeV/u carbon ions
- 300 MeV/u carbon ions
- 135 MeV protons
- 18 MV photons

Graph showing relative dose vs. depth in water (cm).
Adding together Bragg peaks from multiple beam energies with independent weights can generate a flat region at the tumor at the expense of increasing the entrance dose.
Range Scattering with Penetration in Water

\[ \sigma_z = 0.012 * R^{0.951} / A^{1/2} \]
Lateral Scattering with Penetration in Water

\[ \sigma_{xy} = 0.0294 R^{0.896} / A^{0.396} Z^{0.207} \]
Particle Range versus Particle Energy Scaled From Water

\[ R = 30 \text{ g cm}^{-2} \]

- \(^1\text{H}/^4\text{He}\)
- \(^3\text{He}\)
- \(^{12}\text{C}\)
- \(^{16}\text{O} / ^{20}\text{Ne}\)
Dose distribution in micrometer scale

sparsely ionizing photons
densely ionizing particles

X-ray

C 1 MeV/u
LLUMC Facility Layout

The Loma Linda University Medical Center
Proton Treatment Center

Slide courtesy of B. Arjomandy, LLUMC
NPTC Treatment Room
Superconducting Cyclotron for Paul Scherrer Institute (PSI), Villigen, Switzerland
Beam Transfer Line
HIT Heidelberg Ion-beam Therapy
GSI Technology
Siemens Tech Transfer
Dose Distribution Comparison

Protons

Low integral Dose.

90% line

Photons (Tomotherapy)
Comparison study

Relapsing Pituitary Adenoma

Dose distribution in transversal slice

Photons

Protons
A Better Way to Produce $^{99}$Mo (and Other Medical Isotopes)

May 14$^{th}$, 2010—Dr. Gregory Piefer
Overview

1. The Morgridge Institute for Research and Phoenix Nuclear Labs are developing a system to produce reactor grade medical isotopes without a traditional reactor.
2. System is capable of helping end the medical isotope crisis quickly and relatively inexpensively.
3. Technology has two key aspects:
   - Primary neutrons created by high output D-T source
   - Neutrons enter aqueous LEU solution where they multiply subcritically and create medical isotopes.
4. Single device could produce nationally relevant quantities of $^{99}$Mo and other medical isotopes (>40% $^{99}$Mo).
Neutrons are made by reactions between deuterium and tritium atoms

- Deuterium gas flows into ion source, is ionized by RF or microwaves
- Simple DC accelerator pushes ions toward target chamber (300 keV)
- Accelerated deuterons strike tritium gas in target chamber, creating neutrons
- Proof of high efficiency and yield already demonstrated (> $2 \times 10^9$ n/s per watt)
- High energy neutrons allow for (n,2n) multiplication on beryllium
- Only reaction products from this process are neutrons and $^4\text{He}$
**SHINE Driver Specifications**

### Physical
- Consists of two ion injector / accelerator pairs discharging into a common target chamber
- Structure held together with aluminum frame
- Integrated beryllium multiplier ~ 1000 lbs
- Total driver weight ~ 2000 lbs
- Ion source, pumping power supplies, cooling systems fully integrated
- High voltage delivered externally

### Operational
- Deuteron / triton current: 100 mA (50 mA per injector)
- Beam energy: 350 keV
- Beam power: 35 kW
- Neutron output: $5 \times 10^{13}$ n/s (14.1 MeV)
- Tritium inventory: 0.015 g (~ 150 Ci)
- Tritium consumption (per year): 0.007 g (~ 60 Ci)
- Wall power (with pumping): 50 kW
SHINE Overview

- **SHINE** (Subcritical Hybrid Intense Neutron Emitter)
  - Consists of an aqueous pool of uranium nitrate or sulfate
  - Pool driven by 12 D-T drivers
  - Beryllium surrounding pool provides neutron reflection and multiplication
  - Isotopes made from fission of uranium in solution
  - Uranium concentration controlled to keep pool subcritical
  - Solution chamber partitioned so sections may be drained on different days

- **Key Benefits**
  - No criticality
  - No instability as demonstrated with all previous aqueous reactor systems
  - Inherent safety-needs to be driven to operate
  - Greatly reduced nuclear waste-no reactor needed
  - Utilizes low enriched uranium (19.5%)
  - Aqueous process improves chemical extraction efficiency
  - Simplified regulatory approval process
Specifications

• Physical
  – Size: 7m long by 3.5 m diameter
  – Weight: 20 tons
  – Materials: primarily Zircalloy, aluminum, beryllium

• Safety
  – Subcritical, criticality monitored by in-core neutron detectors
  – Large negative power coefficient caused by radiolysis
  – Neutron poisons to be added if criticality exceeds operational limits
  – Dump tank if reactivity exceeds safety thresholds with passive and active valves

• Key parameters
  – Fission power: ~ 250 kW
  – $^{99}$Mo production rate: 2500 6-day kCi / wk
  – Driver neutron production: $6\times10^{14}$ n/s @ 14.1 MeV
  – Driver power consumption: 600 kW
  – Multiplication factor from Be: 2-3
  – Maximum $K_{eff}$: ~ 0.95
  – Neutron flux: ~ $10^{13}$ n/cm$^2$/s average flux in solution
Present Status

• PNL, in collaboration with the Morgridge Institutes for Research, and UW-Madison is seeking $25 M DoE grant to assist with construction of SHINE production facility
• Several key partners secured or in negotiation
  – Los Alamos National Laboratory
  – Lawrence Berkeley National Laboratory
  – TechSource
  – MDS-Nordion
  – GE
  – Lantheus Medical Imaging
  – INVAP-Argentina
• Goal is to commercialize SHINE by Jan. 1, 2014, use revenues to expand into other applications
Keep still; very, very still!