Production* and Applications of $^{211}\text{At}$ at Duke University

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Astatine-211 Production: Current Status

- Internal target
- 28.0 MeV α-particles
- About 1 production run per week
- Max produced: 9.3 GBq
- Typical run: 3 h @ 48 μAp provides ~6.8 GBq EOB
CS-30 has been reliable but is now >35 years old!
Cyclotron Subsystem Updates*

- Under direction of John Vincent – Ionetix

- Completed tasks (selected):
  - replaced air compressor drying system
  - rebuilt existing large cyclotron vacuum valve
  - address cooling water issues
  - obtain spare ion source power supply
  - design new rack for housing power supplies for ion source, deflector dee bias, harmonic trim coils

*Funded by DOE DE-SC0020218
Updates that are in Progress*

- Design/install PLC-based control system with beam current readout
- Design/build new Knob/Meter
- Design/build console control power distribution panel

*Funded by DOE DE-SC0020218
Next Steps and Potential Implications

- Increase α-particle beam energy to 29.0 MeV
  - radionuclidic purity evaluation by TUNL
- Evaluate alternative target geometry
  - head-to-head comparison with current target

**Assumptions:**

1. 3 h@28 MeV = 6.8 GBq; @29 MeV = 14 GBq
2. Automated module: 89% yield purification; 75% yield for synthesis; 1 h total purification/production time = 607 MBq $^{211}\text{At}$-TAT agent per GBq $^{211}\text{At}$ in target
3. Typical patient dose = 370 MBq

Then 3-h run @29 MeV could produce 23 patient doses

Two runs/day, 5 days/week x 50 weeks/year could provide 11,500 patient doses per year
Astatine-211 Projects at Duke

- PSMA inhibitors
- PARP inhibitors
- Gold nanostars
- VHH (nanobodies)
- Next generation labeling technologies
$^{211}$At-Labeled PSMA Inhibitors

<table>
<thead>
<tr>
<th>Tissue</th>
<th>$^{[211\text{At}]}$YC-IV-11</th>
<th>$^{[211\text{At}]}$PSMA-620</th>
<th>$^{[211\text{At}]}$HS-549</th>
<th>$^{[211\text{At}]}$PSMA-904</th>
<th>$^{[211\text{At}]}$VK-02-90-Lu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 h</td>
<td>18 h</td>
<td>1 h</td>
<td>21 h</td>
<td>1 h</td>
</tr>
<tr>
<td>Tumor</td>
<td>17.9±3.0</td>
<td>31.1±9.8</td>
<td>16.5±4.8</td>
<td>13.6±3.3</td>
<td>43.2±9.8</td>
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<tr>
<td>Kidneys</td>
<td>72±12</td>
<td>57±7</td>
<td>103±24</td>
<td>7.5±1.8</td>
<td>47±8</td>
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<tr>
<td>Stomach</td>
<td>10.1±1.7</td>
<td>9.4±3.0</td>
<td>2.0±0.4</td>
<td>1.9±1.0</td>
<td>7.1±2.2</td>
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At-VK-02-90 Single Dose Efficacy Studies

Subcutaneous Model
PSMA+ PC3-PIP
PSMA- PC3 flu

Metastatic Model
PC3-ML-Luc
Monitored by BLI imaging

No toxicities observed in 13-month MTD study with CD-1 mice at therapeutic dose doses

Figure 4. Therapeutic efficacy of $[^{211}\text{At}]VK-02-90$ in subcutaneous (A) and metastatic models of prostate cancer (B).
Gold Nanostars for $^{211}$At Delivery

We have used star-shaped gold nanoparticles, gold nanostars (GNS), as a new strategy for $^{211}$At delivery. Experiment results demonstrated that the $^{211}$At labeling on GNS can be achieved with high efficiency in a short time. In addition, labeled $^{211}$At on GNS has high stability with minimal dissociation when incubated in PBS or serum up to 24 h at 37 °C.
**211^At-GNS: In Vivo Results**

### Tissue % ID Results

<table>
<thead>
<tr>
<th>Tissue</th>
<th>%ID 30 min</th>
<th>%ID 2 h</th>
<th>%ID 14 h</th>
<th>%ID 21 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>0.61 ± 0.21</td>
<td>0.64 ± 0.28</td>
<td>0.44 ± 0.18</td>
<td>0.61 ± 0.21</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.21 ± 0.06</td>
<td>0.28 ± 0.08</td>
<td>0.43 ± 0.14</td>
<td>0.49 ± 0.10</td>
</tr>
</tbody>
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**Prolonged vascular residence time**

**Low deestatination in vivo**

IT therapy in U87MG glioma model (n=10) @ 1.11 MBq dose
**Nanobody™/VHH/sdAb**

- **Derived from camelids**
- **Smallest fully functional fragment from a natural single chain Ab**
Treatment of BT-474 Breast Carcinoma Xenografts with Single Dose $iso-[^{211}\text{At}]SAGMB-5\text{F7 VHH}$
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