Commissioning an IRay System for ocular stereotaxy using Integrated Tissue Air Ratio

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Oraya Therapeutics, Inc.
Overview

IRay System and wet AMD
ITAR Dosimetry Method
In the USA the IRay® Radiotherapy System is an investigational device and is not available for sale.
Wet Age-related Macular Degeneration

Leading cause of vision loss for people over the age of 50

200,000 new cases of wet AMD in the USA every year

No cure – current standard of care is as-needed injections of anti-VEGF
Dose Distribution and Immobilization

Gy per second
- 5e-7
- 5e-6
- 5e-5
- 5e-4
- 5e-1

Log (common) scaling
Radiotherapy for wet AMD

**History**

Started ~25 years ago and continuing

EBRT and GKS attempted

Typical pilot study:

10-20 Gy in 2-3 Gy fractions

**Most promising studies:**

Bergink *et al*: 24 Gy in 4 fractions

Char *et al*: 7.5 Gy in single fraction

Avila *et al* (2): 24 Gy in single fraction

**Clinical Rationale**

Anti-angiogenic – preferentially destroys neovasculature

Anti-fibrotic – microfibroblast apoptosis

Anti-inflammatory – reduction in cellularity infiltrate

Pericyte knockdown in mature vessels – re-exposes VEGF receptors
Oraya Therapy

16 Gy in 1 fraction
<0.4 mSv effective dose
Non-invasive
~4 min x-ray time
INTREPID Clinical Trial

Randomized, sham-controlled, double blind study of the effect of low-energy X-ray in sparing anti-VEGF injections

Study population: **Non-Naïve** (≥3 inj.) wet AMD patients with persistent or recurrent disease activity

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Primary endpoint = # Injections
Secondary endpoint = VA
Safety Assessments
51% of best responders received a mean of 1 injection over 2 years. Vision in SRT group 4.4 letters superior to control group (P = 0.23).
ITAR Dosimetry Method
Hanlon et. al., Med Phys 41, 021729 (2014)
Dosimetry for IRay System

**Oraya beam:**
- 100 kVp
- 4.2 mm spot size at isocenter
- 150 mm SAD
- 16 to 26 mm depth of interest
- ~3.4% falloff per mm at depth

**Challenge:**
Dearth of suitable detectors
\( P_{q,\text{cham}} \) unknown for suitable detectors

**TG-61 requirements:**
- Water phantoms over plastic
- Air filled detectors with energy-independency <2%
ITAR solution

$R^2$
Dominant effect
Measure directly

**Attenuation**
Secondary effect
Measure directly

**Scatter**
Third order effect
MCNP
\[
LSTAR(d) = \frac{\dot{K}_{\text{air}, z=d}(d)}{\dot{K}_{\text{ref}}} = \alpha \exp(-\beta \times d)
\]

\[
\text{ITAR}(d) = \alpha \exp(-\beta \times d) \times C_{\text{mat}} \times C_{\text{scat}}(d) = A \exp(-B \times d)
\]
C_{mat}
LSTARs for $C_{\text{mat}}$
$C_{\text{scat}}$ tally volume
C_{scat}

<table>
<thead>
<tr>
<th>depth (cm)</th>
<th>C_{scat}(d)</th>
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<tr>
<td>1.6</td>
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<tr>
<td>1.8</td>
<td>1.103</td>
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<td>2.0</td>
<td>1.104</td>
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<td>2.2</td>
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<td>1.105</td>
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<tr>
<td>2.6</td>
<td>1.106</td>
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\[ C_{scat}(d,x) = y_0 + a \times \exp(-b \times x) \]
where \( x \) = Tally Cylinder Thickness
**Commissioning Sample**

### LSTAR Measurements

<table>
<thead>
<tr>
<th>d (mm)</th>
<th>Temp (°C)</th>
<th>Press (mbar)</th>
<th>PFP</th>
<th>Rdg (µA)</th>
<th>M (pA)</th>
<th>CV (%)</th>
<th>M_air=d (d)</th>
<th>LSTAR(d) (Gy/min)</th>
<th>n/a</th>
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<tr>
<td>0</td>
<td>24.2</td>
<td>1023.6</td>
<td>0.997</td>
<td>25.705</td>
<td>25.705</td>
<td>0.03</td>
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<td>18.033</td>
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<td>0.998</td>
<td>12.099</td>
<td>12.099</td>
<td>0.04</td>
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\[ LSTAR(d) = \alpha \exp(\beta \cdot d) \]

- \( \alpha = 0.8805 \) (n/a)
- \( \beta = 0.0347 \) (1/mm)

### ITAR Conversion

<table>
<thead>
<tr>
<th>d (mm)</th>
<th>LSTAR(d)</th>
<th>( C_{\text{mat}} )</th>
<th>( C_{\text{cat}} )</th>
<th>( \text{ITAR(d)} )</th>
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<tr>
<td>16</td>
<td>0.5055</td>
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<td>0.3831</td>
<td>1.019</td>
<td>1.105</td>
<td>0.4313</td>
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</table>

\[ \text{ITAR(d)} = A \exp(-B \cdot d) \]

- \( A = 0.9832 \) (n/a)
- \( B = 0.0343 \) (1/mm)

\[ D_{\text{macula(TPL)}} \xrightarrow{\text{CPE}} K_{\text{ref}} \times \text{Output Factor} \times A \exp(-B \cdot TPL) \times \left( \frac{\bar{\mu}_\text{en}}{\rho} \right)^w_{\text{air}} \]
Comparison to traditional TAR

Easier to setup clinically

Field size independent – interesting for other applications?

Difficult to compare because of $P_{q,cham} \rightarrow$ AAPM
Other commissioning and Self Test
Other commissioning and Self Test
Survey Map

All values in $\mu$Sv/hr

Values represent scatter rates during treatment

Each treatment is ~4 minutes so average dose rate is much lower
Commercial strategy with clinical medical physicists

Commission during acceptance testing
Share data and methods with local physicists
Support further commissioning activities if necessary
Conclusions

IRay System and Oraya Therapy
INTREPID clinical trial results good
Currently available in the UK, Germany, and Switzerland

ITAR Dosimetry Method for Commissioning
Easy to measure clinically
More conceptually abstract than traditional TAR