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

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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

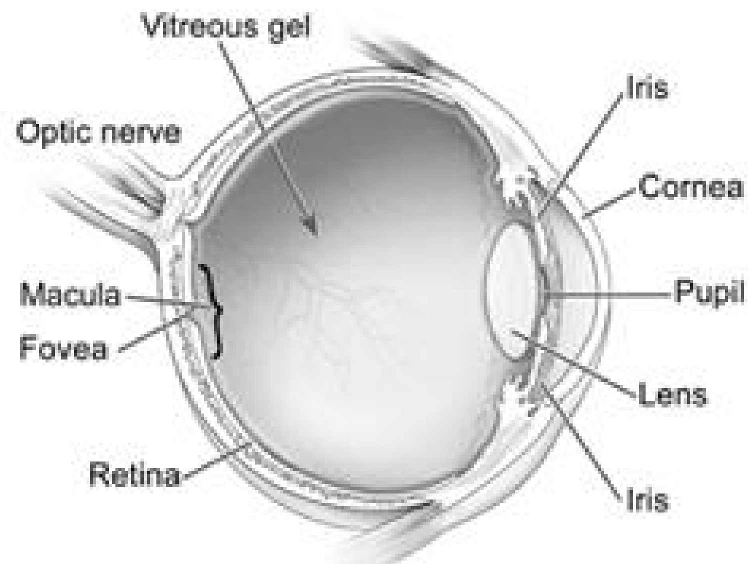
IRay System

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

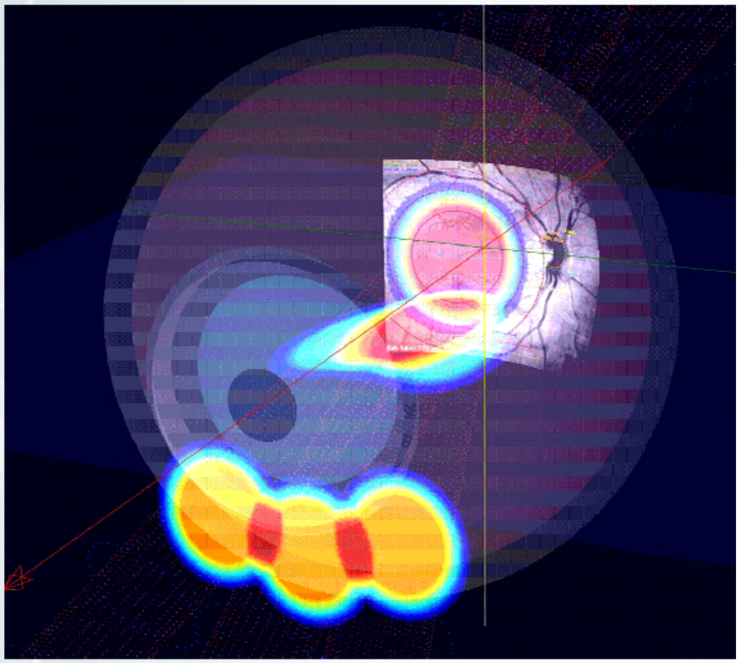


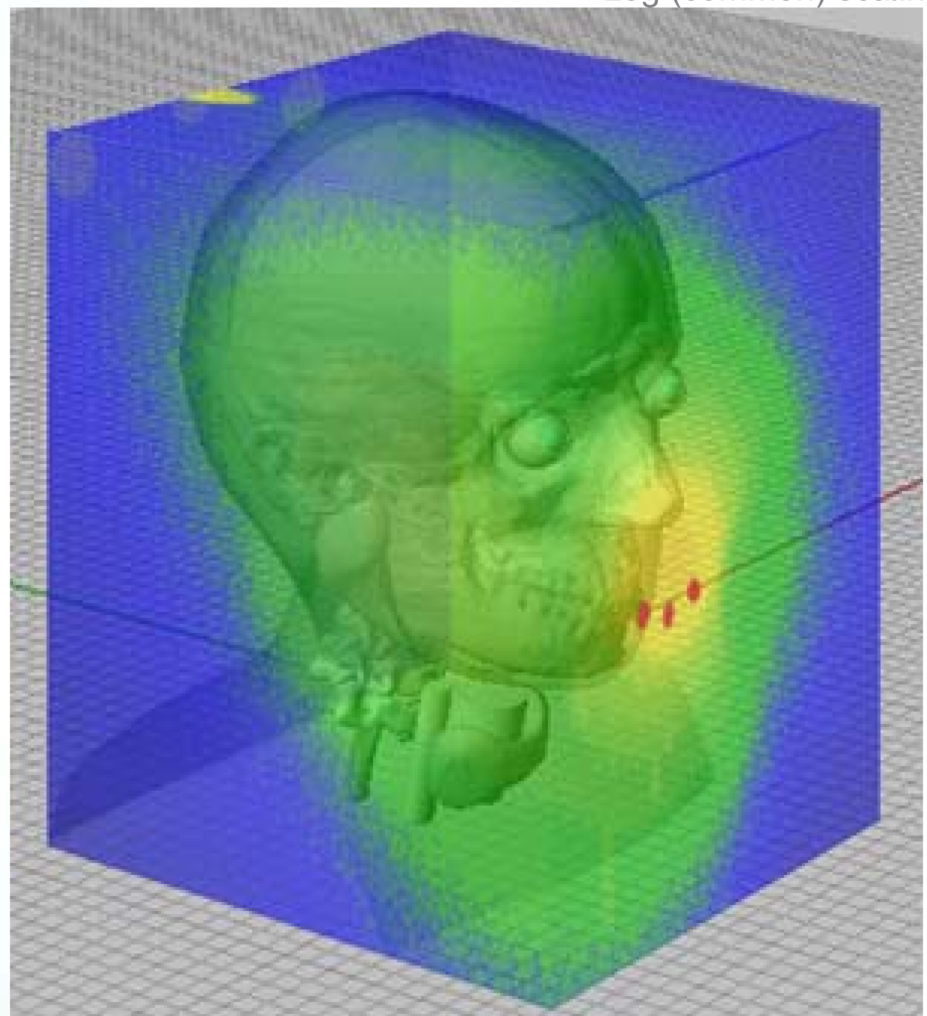
Dose Distribution and Immobilization

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

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Oraya Therapy

16 Gy in 1 fraction

<0.4 mSv effective dose

Non-invasive

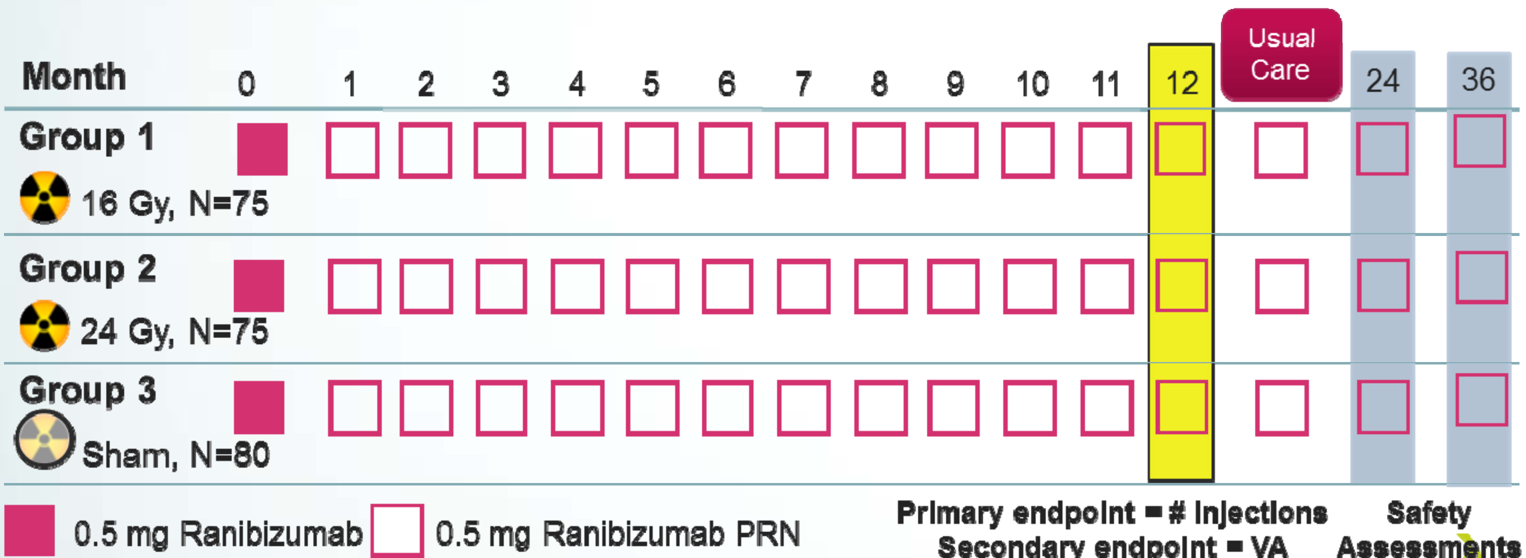
~4 min x-ray time

Axial

INTREPID Clinical Trial

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

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



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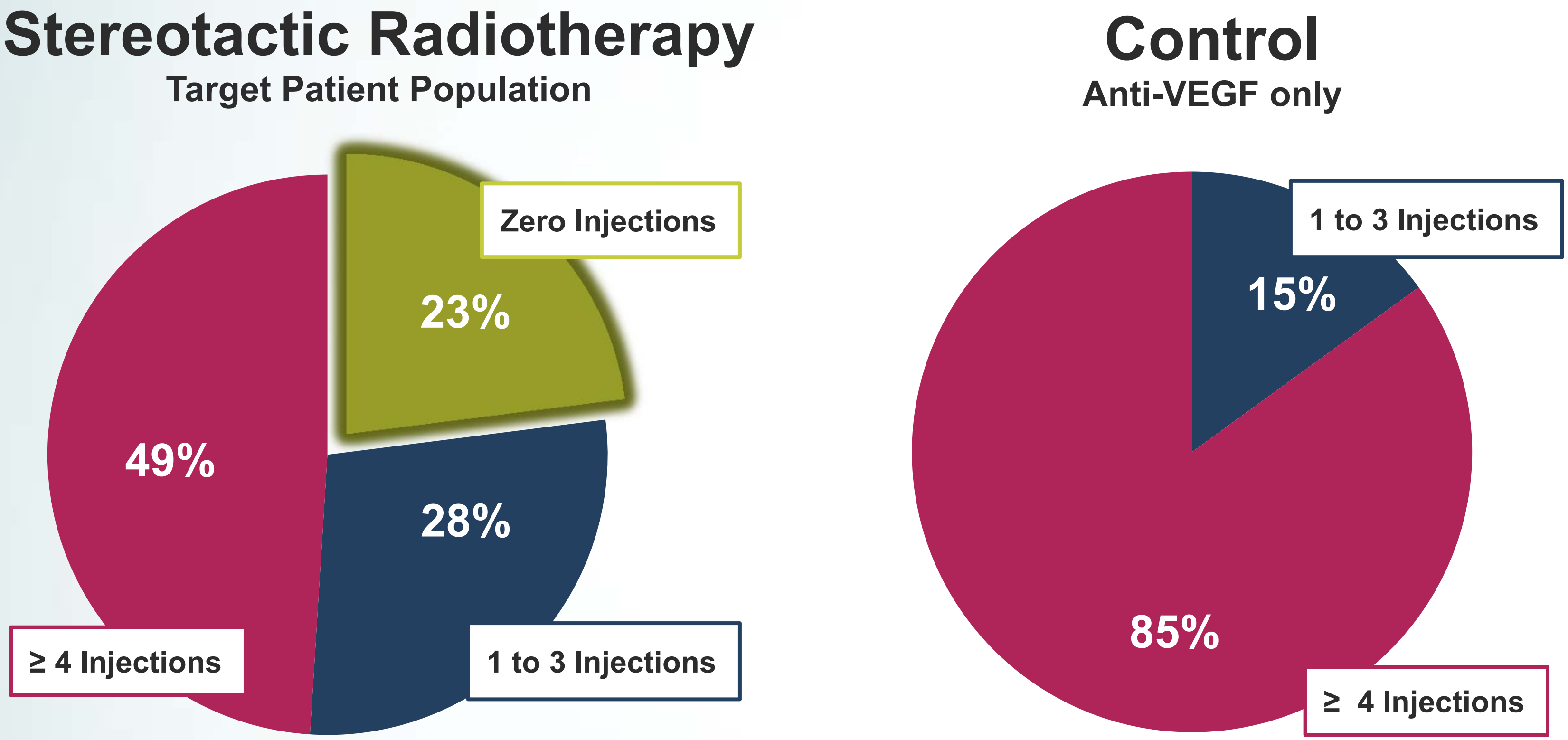
Target Population Differential Response at Year 2



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)

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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

$P_{q,cham}$ unknown for suitable detectors

TG-61 requirements:

Water phantoms over plastic

Air filled detectors with energy-independency <2%

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ITAR solution

R^2

Dominant effect

Measure directly

Attenuation

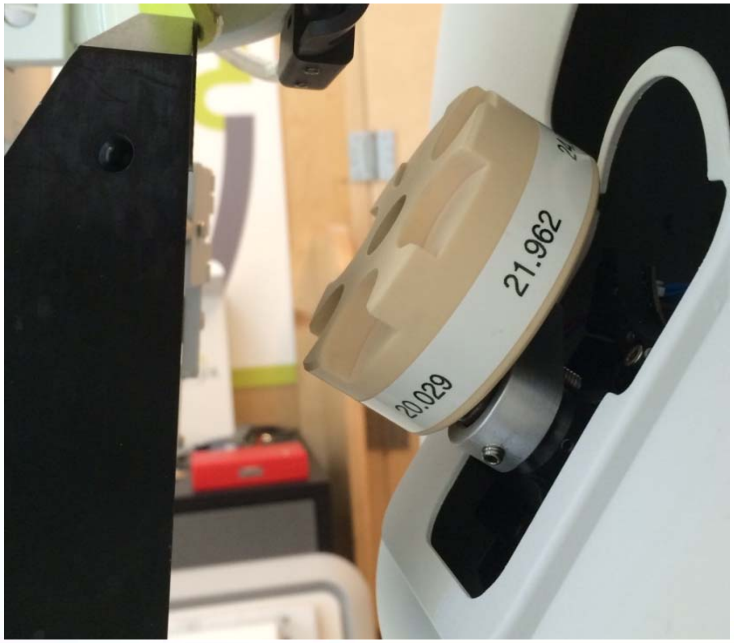
Secondary effect

Measure directly

Scatter

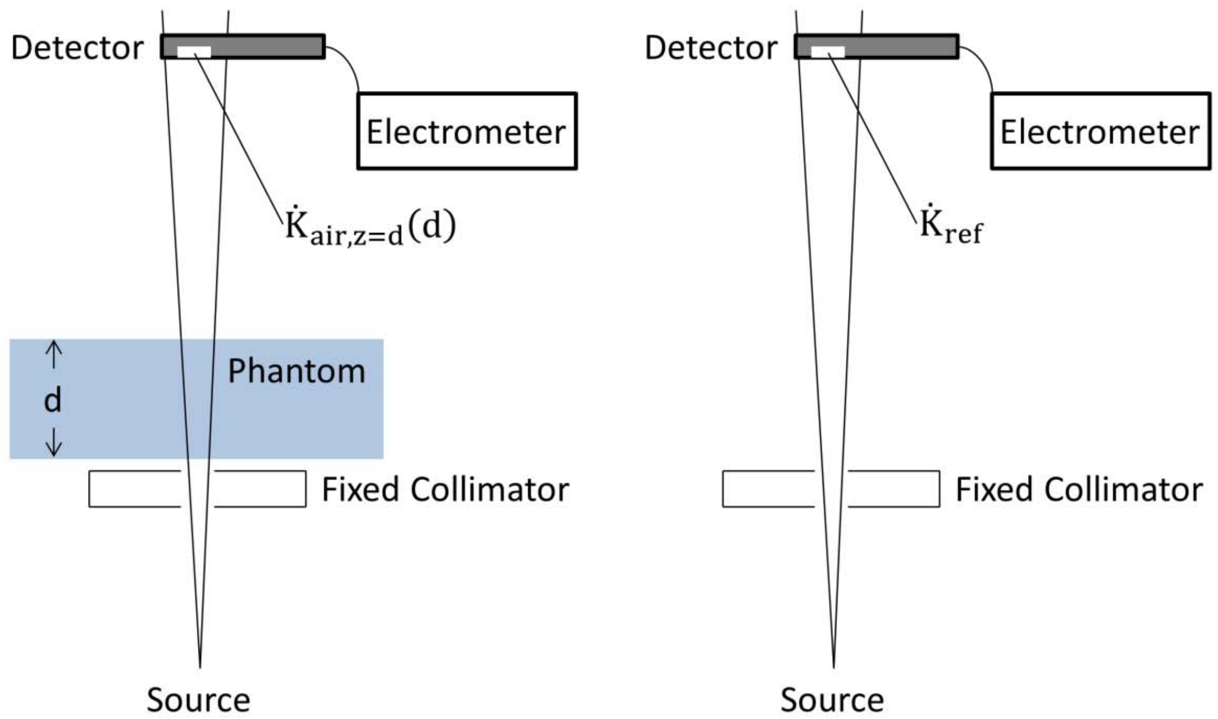
Third order effect

MCNP



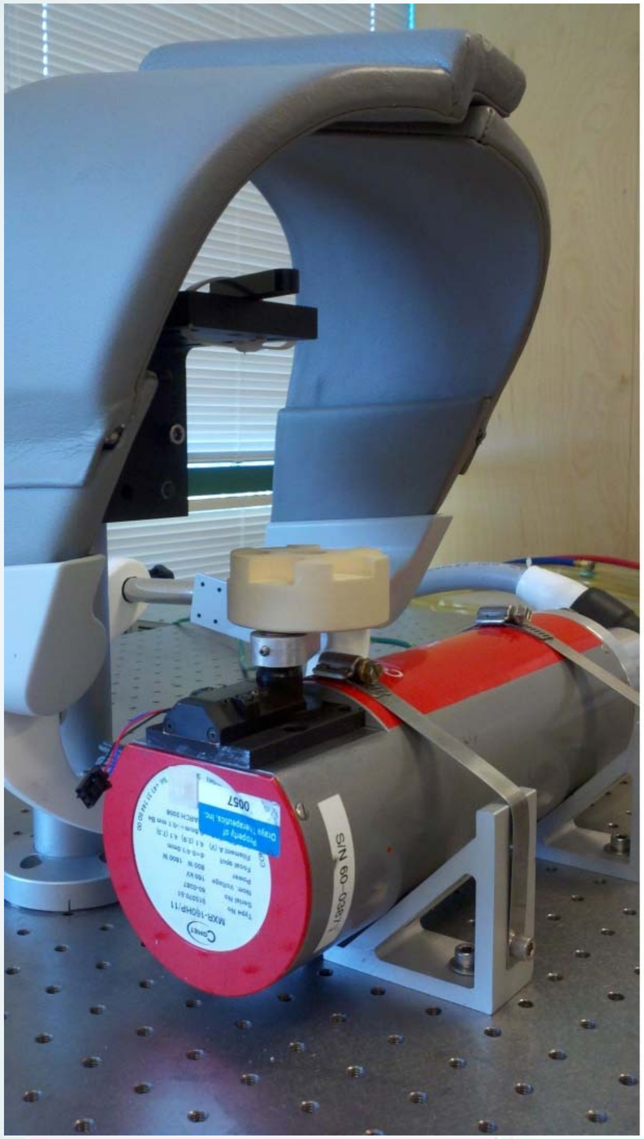
LSTAR

$$\mathrm{LSTAR}(d) = \frac{\dot{K}_{air,z=d}(d)}{\dot{K}_{ref}} = \alpha \exp(-\beta * d)$$

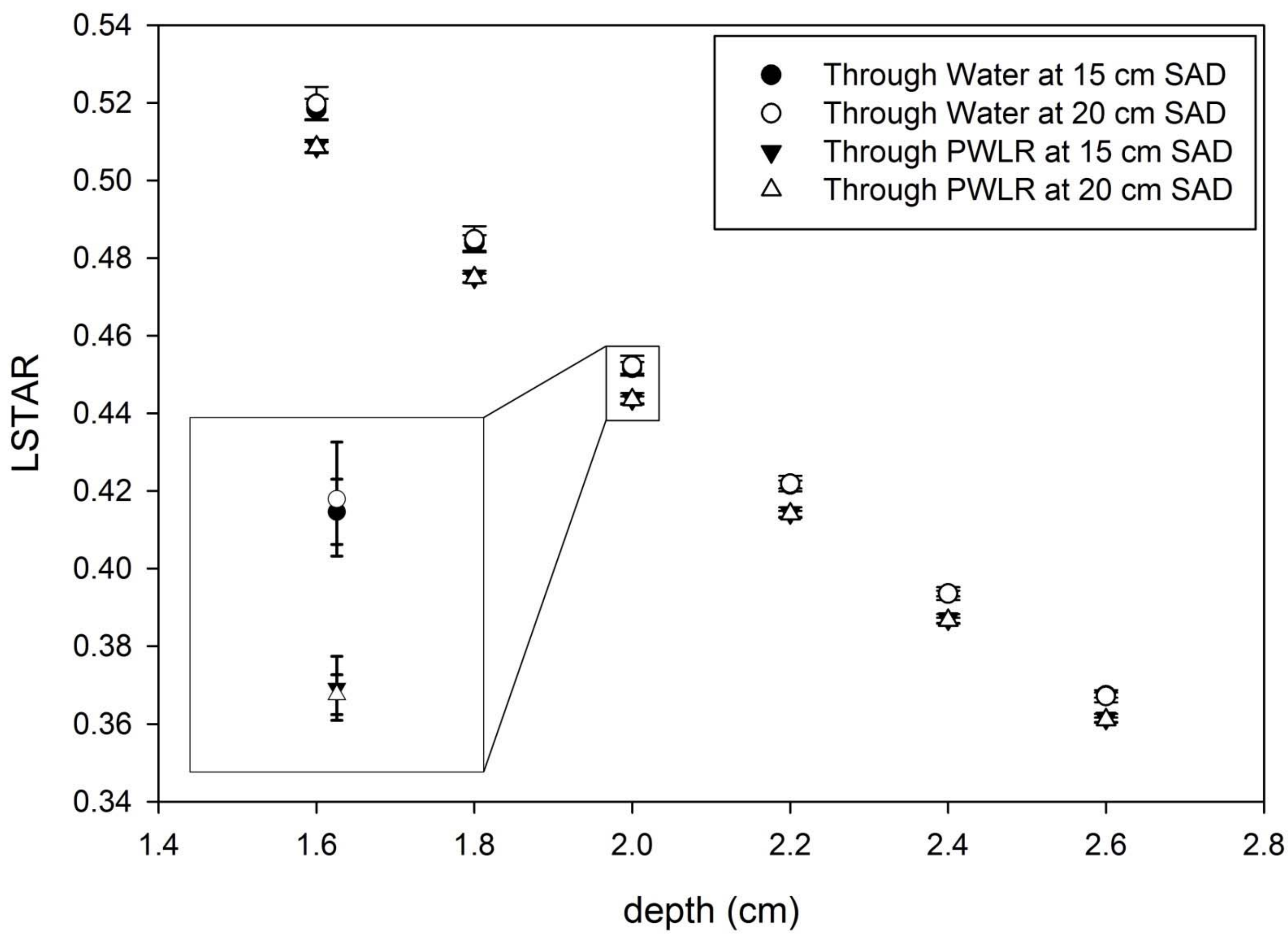


$$\mathrm{ITAR}(d) = \alpha \exp(-\beta * d) * C_{mat} * C_{scat}(d) = A\exp(-B * d)$$

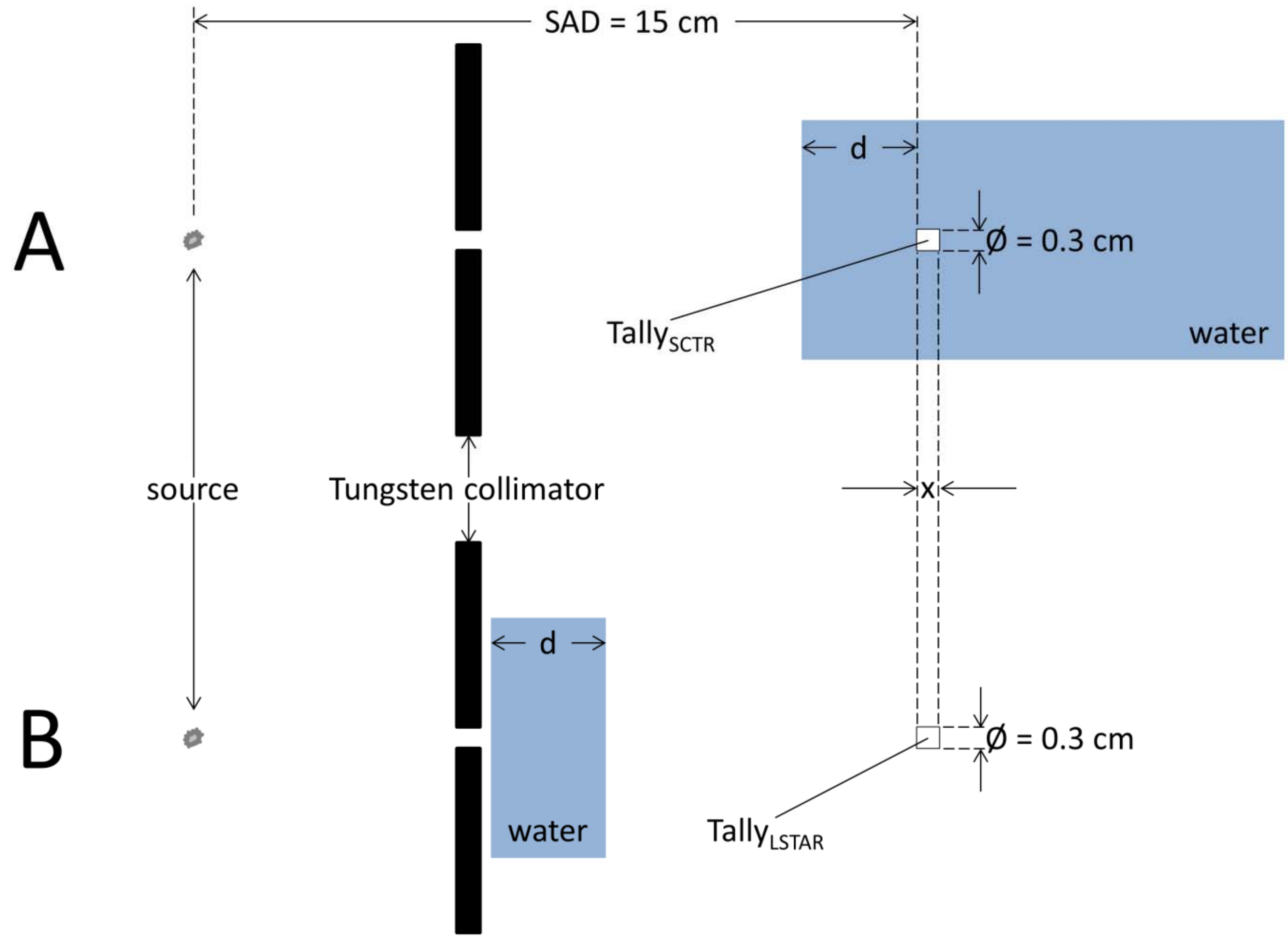
C_{mat}



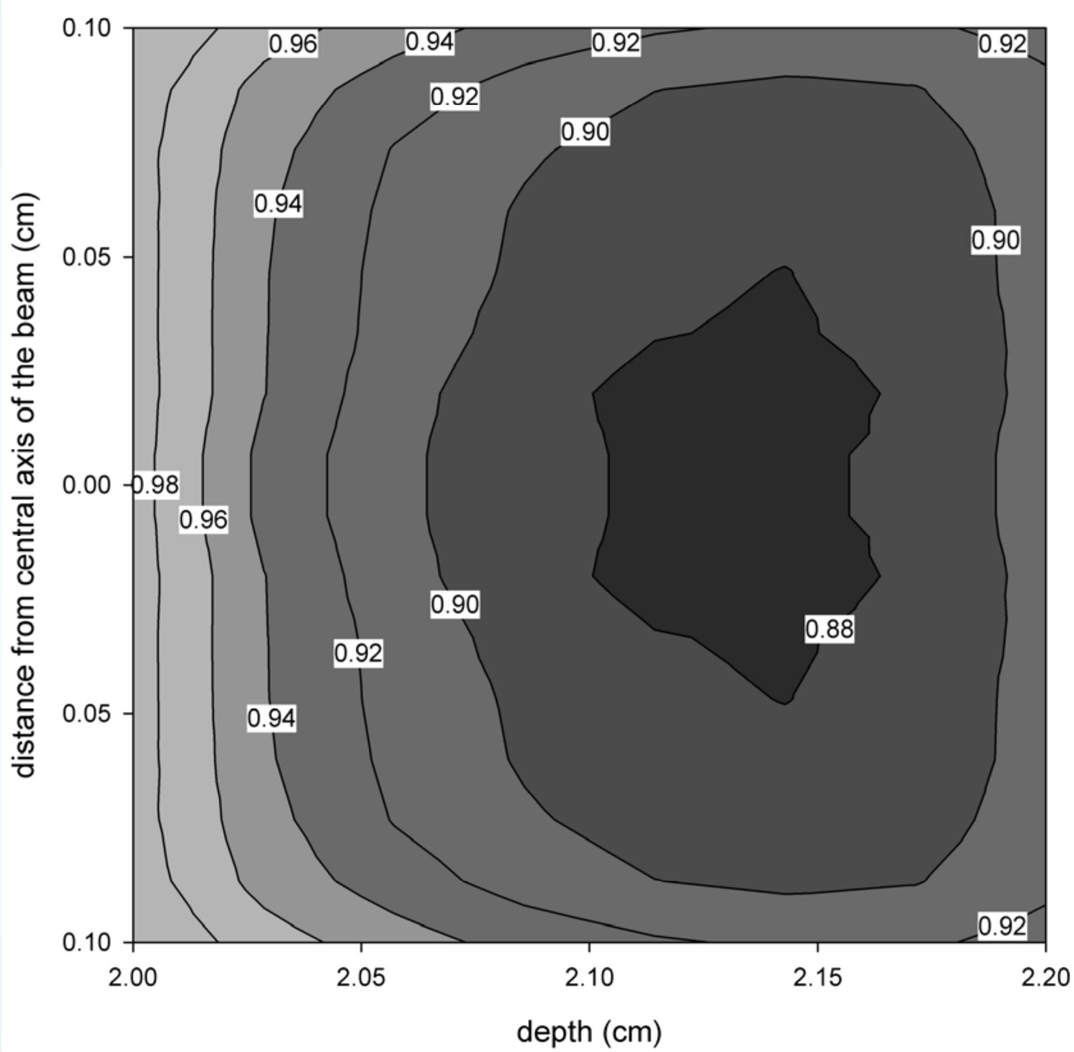
LSTARs for C_{mat}



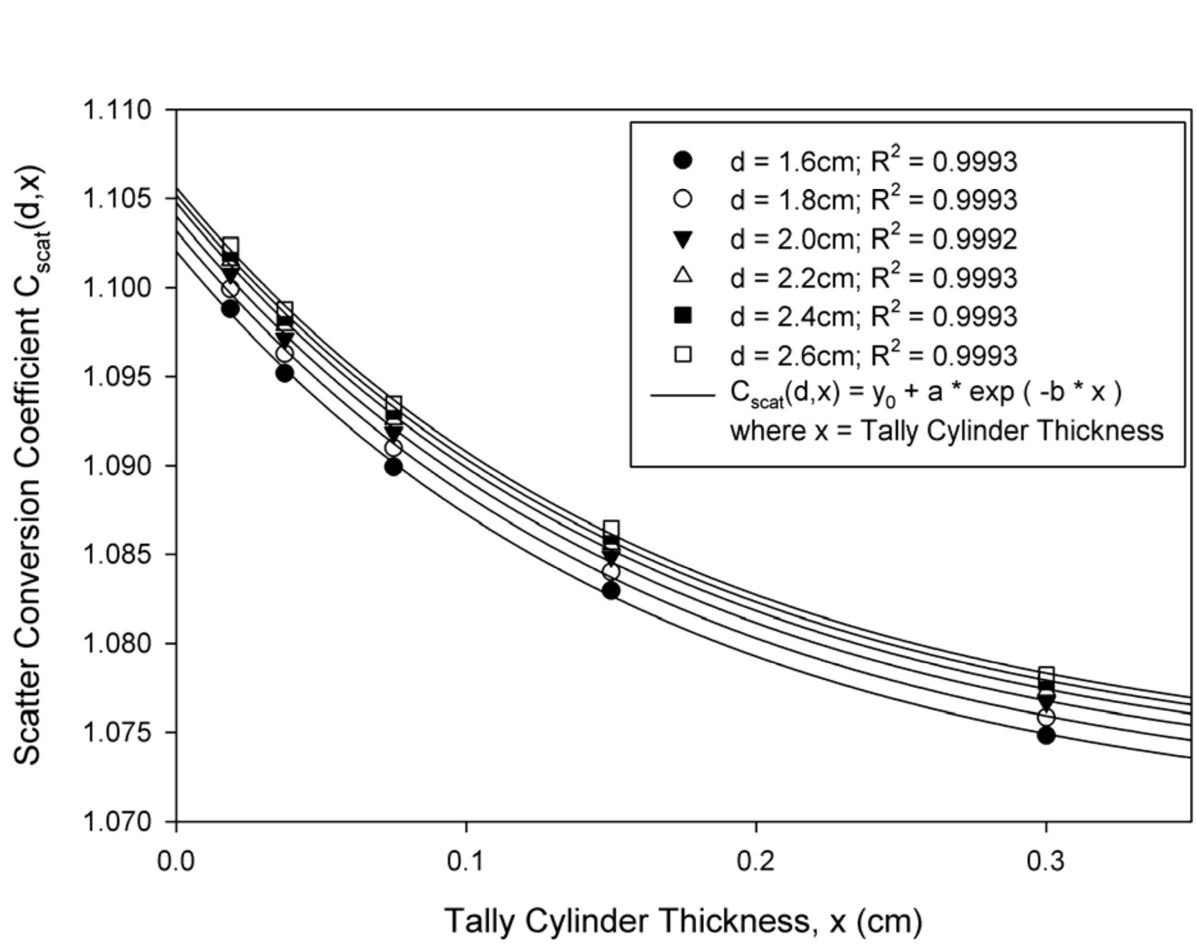
C_{scat}


SAD = 15 cm
A
B
d
d
Ø = 0.3 cm
Ø = 0.3 cm
Tally$_{SCTR}$
Tally$_{LSTAR}$
water
water
source
Tungsten collimator
x

C_{scat} tally volume



C_{scat}



depth (cm)	$C_{scat}(d)$
1.6	1.102
1.8	1.103
2.0	1.104
2.2	1.105
2.4	1.105
2.6	1.106

Commissioning Sample

LSTAR Measurements

kV	mA	Ramp Down	SDD	Rdg Samples	Rdg Time
100	16	1 sec	150 mm	60	30 sec

d	Temp	Press	P_{TP}	Rdg	$\dot{M}_{raw}$	CV	$\dot{M}$	$\dot{K}_{air,z=d}(d)$	LSTAR(d)
(mm)	(°C)	(mbar)	n/a	(pA)	(pA)	(%)	(pA)	(Gy/min)	n/a
0	24.2	1023.6	0.997	25.705	25.705	0.03	25.61	8.702	1.000
16.007	24.2	1023.5	0.997	13.015	13.015	0.02	12.97	4.406	0.5064
18.033	24.2	1023.4	0.998	12.099	12.099	0.04	12.06	4.097	0.4708
20.048	24.2	1023.4	0.998	11.262	11.262	0.03	11.22	3.813	0.4382
21.999	24.2	1023.5	0.997	10.549	10.549	0.02	10.51	3.571	0.4104
24.043	24.2	1023.6	0.997	9.849	9.849	0.03	9.81	3.334	0.3832

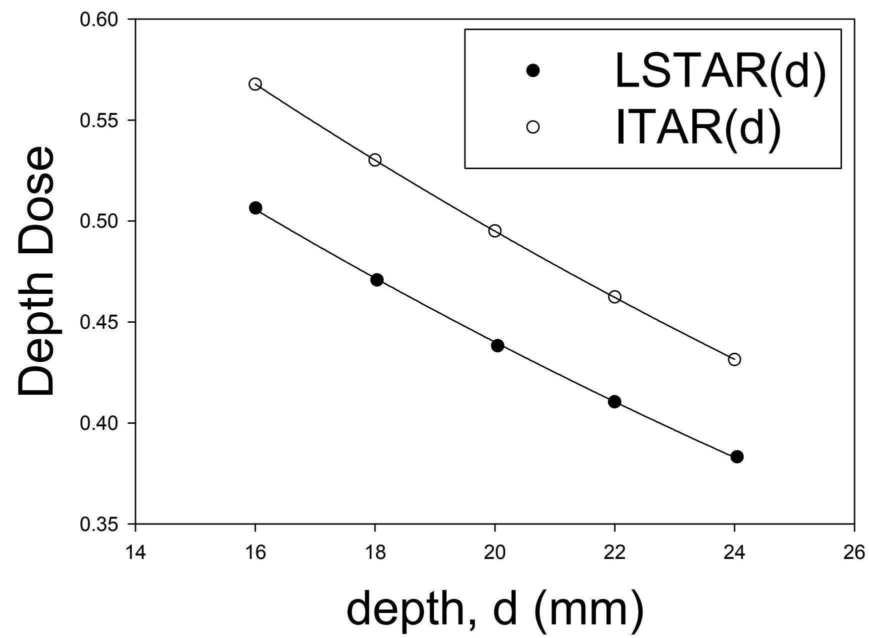
$\dot{K}_{ref} = \dot{K}_{air,z=0} =$ 8.702 (Gy/min)

LSTAR(d) = αexp(-β * d)		
α:	0.8805	(n/a)
β:	0.0347	(1/mm)

ITAR Conversion

d	LSTAR(d)	C_{mat}	C_{scat}	ITAR(d)
(mm)	n/a	n/a	n/a	n/a
16	0.5055	1.019	1.102	0.5677
18	0.4717	1.019	1.103	0.5301
20	0.4401	1.019	1.104	0.4951
22	0.4106	1.019	1.105	0.4623
24	0.3831	1.019	1.105	0.4313

ITAR(d) = Aexp(-B * d)		
A:	0.9832	(n/a)
B:	0.0343	(1/mm)



$$\dot{D}_{macula}(TPL) \overset{CPE}{\Longleftrightarrow} \dot{K}_{ref} * \text{Output Factor} * A\exp(-B * TPL) * \left[\left(\frac{\bar{\mu}_{en}}{\rho}\right)^{w}_{air}\right]_{w}$$

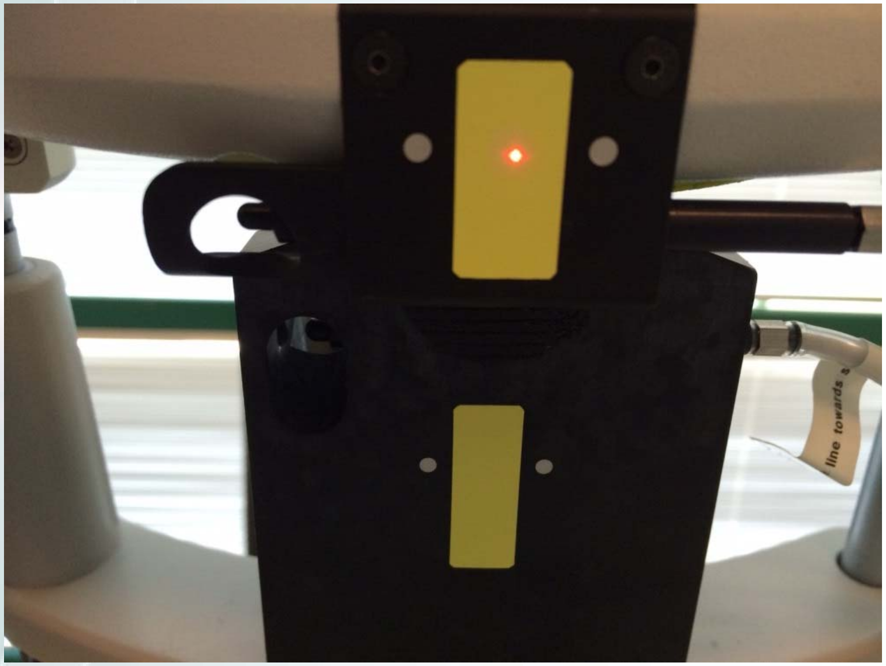
Comparison to traditional TAR

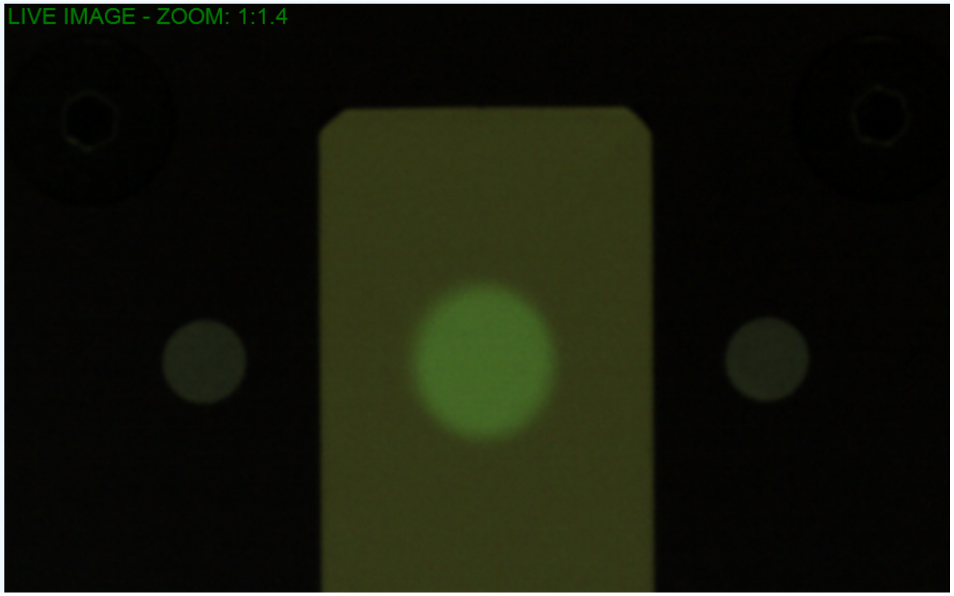
Easier to setup clinically

Field size independent – interesting for other applications?

Difficult to compare because of $P_{q,cham}$ → AAPM

Other commissioning and Self Test





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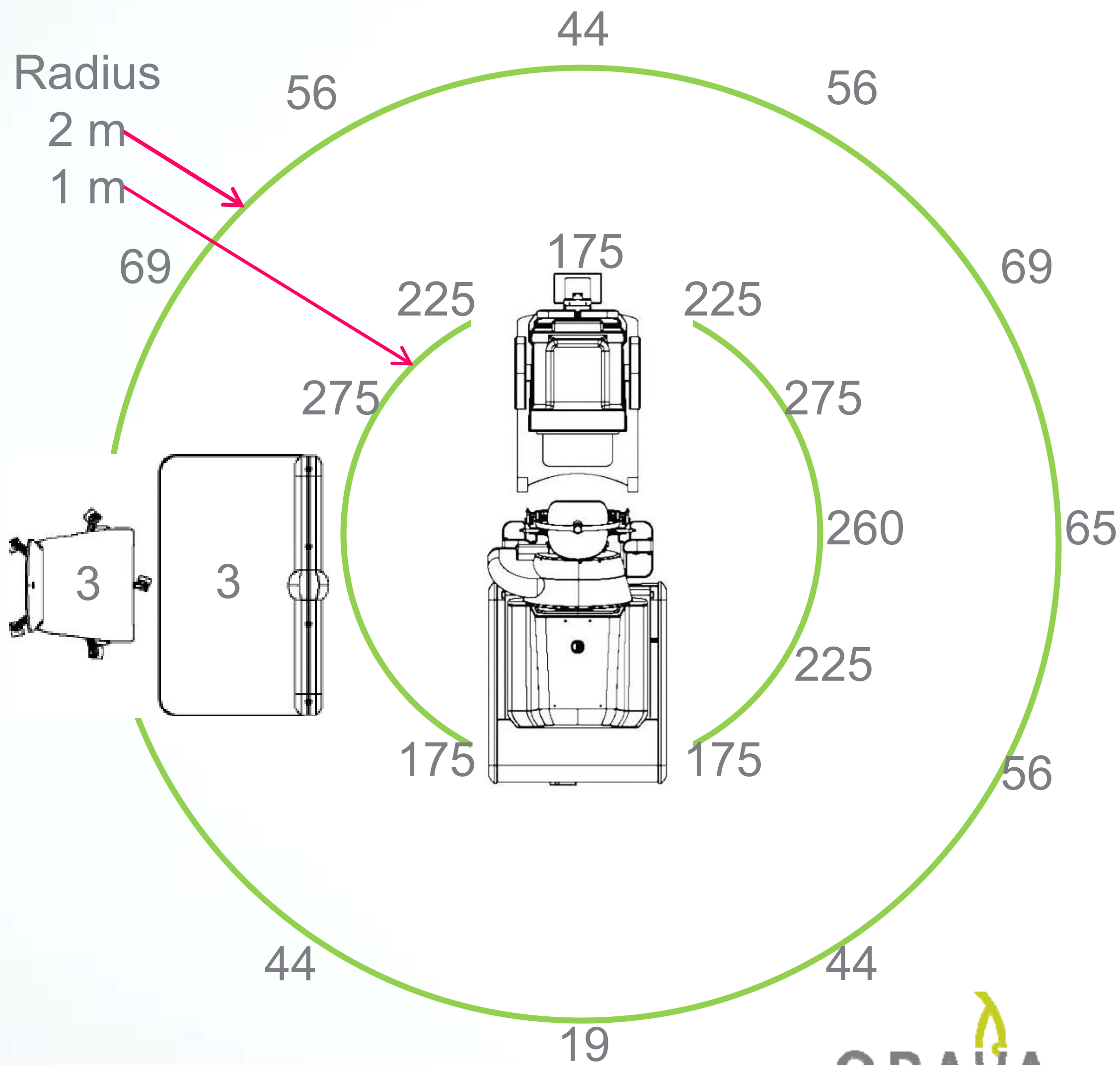
Other commissioning and Self Test

Survey Map

All values in μSv/hr

Values represent scatter rates during treatment

Each treatment is ~4 minutes so average dose rate is much lower



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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