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The current state of physics and dosimetry reporting in radiation biology

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Purpose

- Much recent discussion concerning lack of reproducibility and replicability in science at large
- Estimated 28 billion dollars /year (~50%) spent on irreproducible pre-clinical research (Freedman *et al*, 2015)
- Radiation Biology significant in pre-clinical research
  - Biological effect **Dose-Relationship Curves** depend highly on **amount**, **rate**, and **quality** (type) of radiation delivered
  - Physics & Dosimetry **experimental details** must be **reported** for experiment to be **replicable**, **interpretable**, and **credible**

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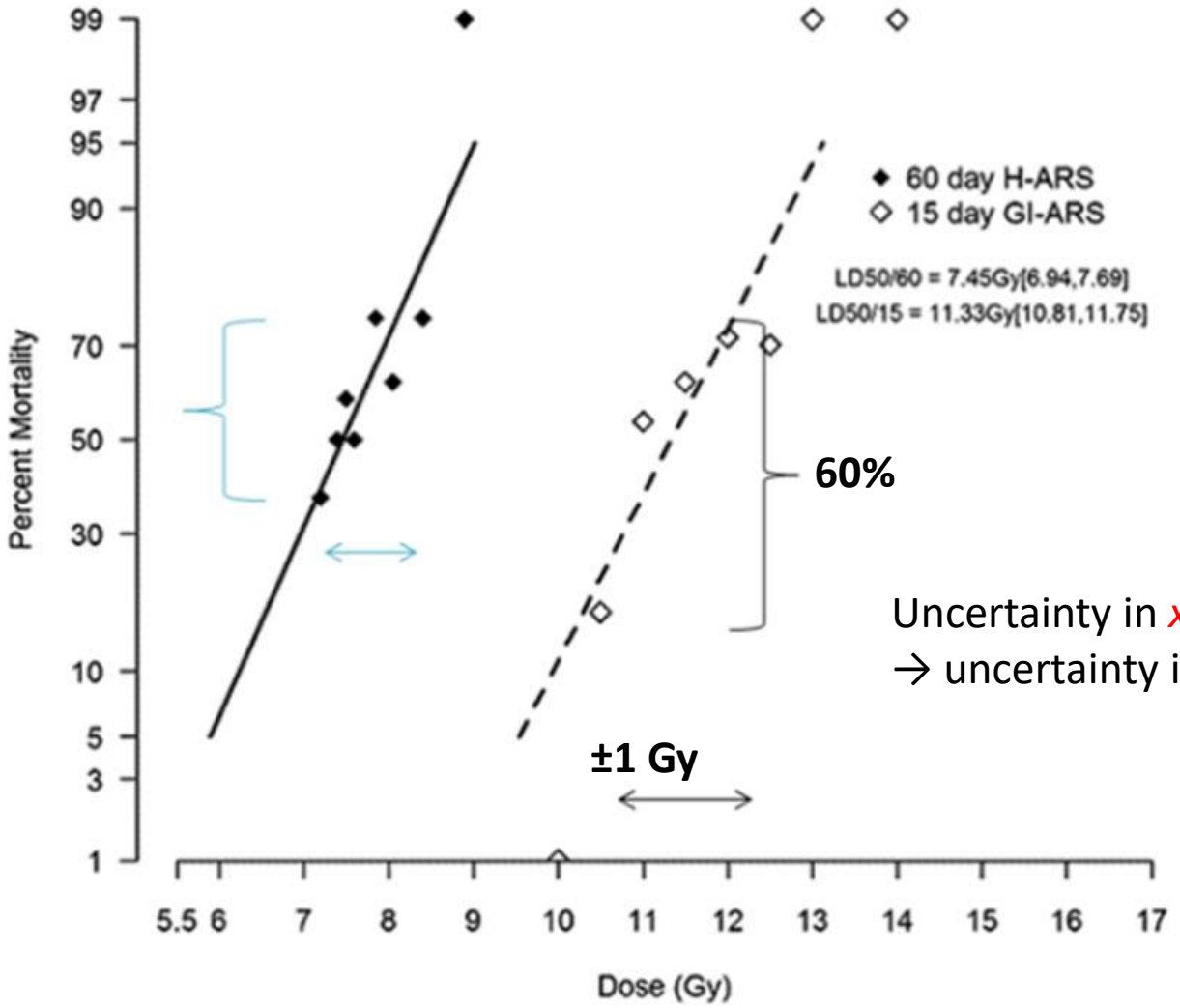
Dose-effect relationship

Radiation dose-effect curves have *steep slopes*



Uncertainty in *x axis* (dose)
→ uncertainty in *effect*

Kazi *et al*, The MCART Radiation Physics Core: The Quest for Radiation Dosimetry Standardization, Health Phys 2014 106(1) 97-105

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Factors influencing **biological effect** :

Amount of Radiation

-Absorbed **dose**

-Dose **rate**

Quality of Radiation

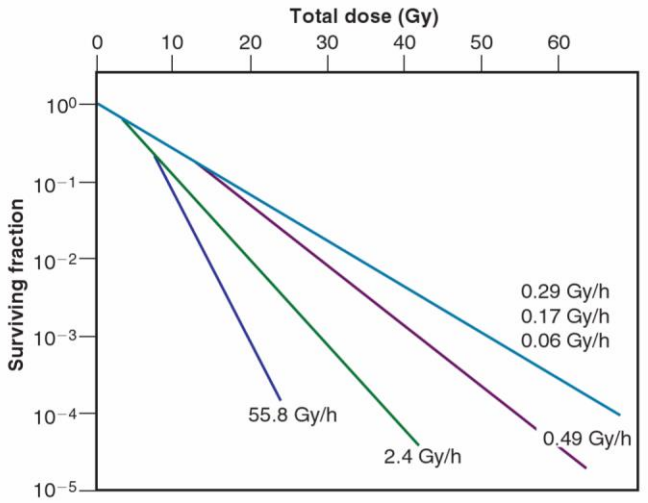
-Particle **type** ($\alpha, \beta, \gamma, p^+, x\text{-}ray$)

-Particle **energy** ($\mathrm{keV} \rightarrow \mathrm{GeV}$)

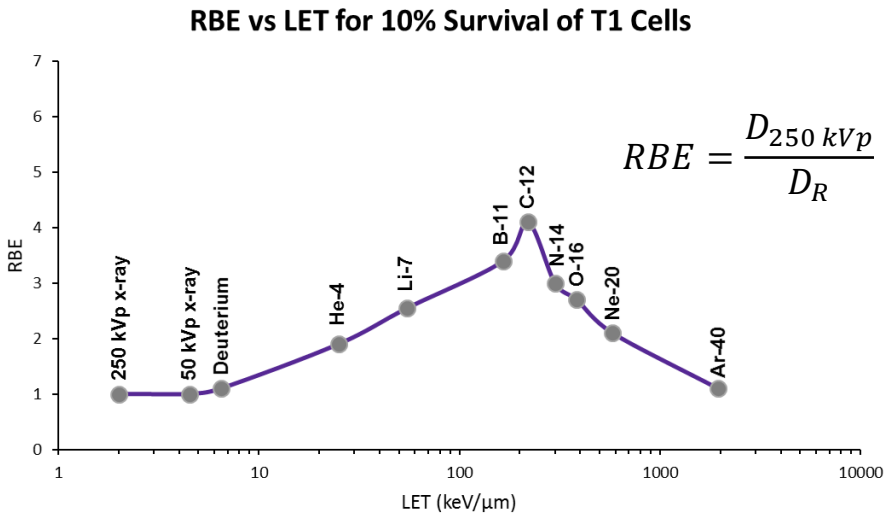
Irradiation *Geometry*

-Calibration vs irradiation conditions

-Attenuation conditions

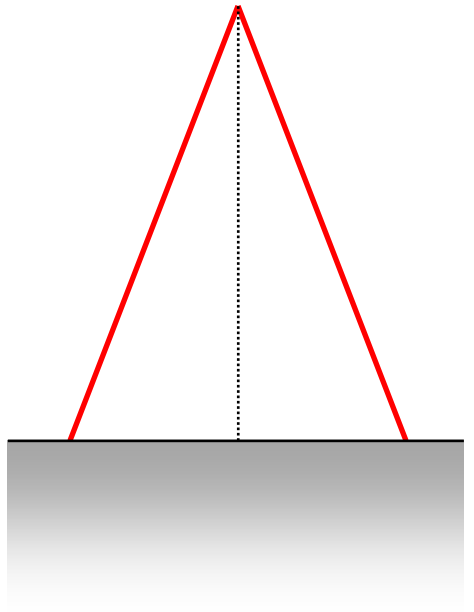


Zeman et al, **Biological Basis of Radiation Oncology**, Clinical Radiation Oncology 2012, 3-42



$$RBE = \frac{D_{250\ kVp}}{D_R}$$

Todd et al, **Heavy-ion irradiation of cultured human cells**, Rad Res Sup 54, 196-207 (1967)



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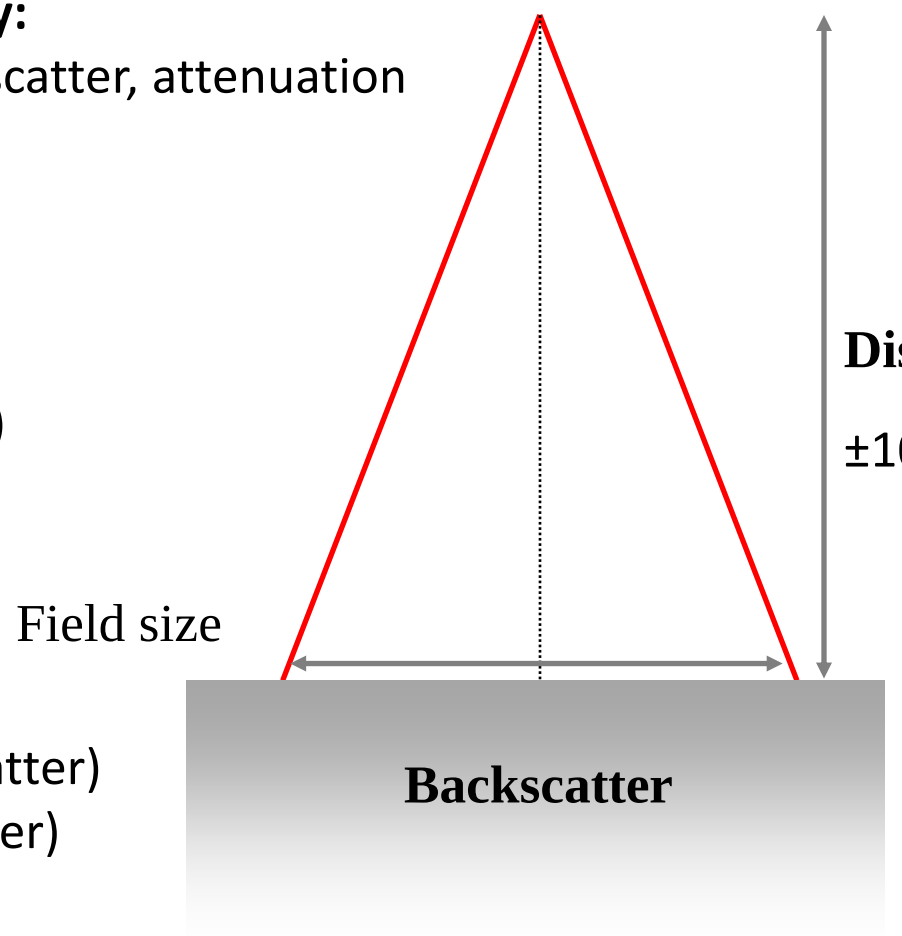
Effect of **Irradiation Geometry**

Beam quality:
Affects backscatter, attenuation

Attenuation:
2%/cm (18 MV)
10%/cm (80 kVp)



Distance ($\sim 1/r^2$)

±10 cm over 50 cm
= ±**45%** dose

Field size
= ±**5%** dose (no backscatter)
= ±**40%** dose (backscatter)

Presence/absence of **backscatter**
= ±**40%** dose

Medium used for dose specification:
-Exposure / Air Kerma?
-Surface of semi-infinite phantom?
-Dose to tissue?

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The Importance of Dosimetry Standardization in Radiobiology

Marc Desrosiers[1], Larry DeWerd[2], James Deye[3], Patricia Lindsay[4], Mark K. Murphy[5], Michael Mitch[1], Francesca Macchiarini[6], Strahinja Stojadinovic[7], and Helen Stone[3]

Volume 118 (2013) http://dx.doi.org/10.6028/jres.118.021

Journal of Research of the National Institute of Standards and Technology

- NIST hosted a symposium in 2012 to identify the key elements to be recorded in Radiation biology
  - Attended by representatives from NIAID, NIST, MCART, NCI, NASA

- Recommendations were published 5 years ago
  - How does the field perform vs those expectations?

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Previous survey on NIST survey implementation

Table 1. The approximate rate of occurrence of specific information within **15 issues** covering March **2010** through March 2011, articles in the journal **Radiation Research**

Animal/Cell type	100 %
Animal/Cell strain	100 %
Irradiator Manufacturer/Model	80 %
Source (nuclide, HVL, filtering)	100 %
Radiation Energy	78 %
Irradiation Geometry*	48 %
Dosimetry Method	37 %
Dose (relative to water, tissue?)	94 %
Dose Rate (fractionated?)	81 %
Location of Detector	20 %
Dose Reference Location	7 %
Published Standards/Guides Used	7 %
Uncertainty in Dose	4 %

Desrosiers et al., **The importance of Dosimetry Standardization in Radiobiology**, Journal of Research of the National Institute of Standards and Technology 118, 403-418 (2013)

One journal, one year

TABLE 1
A Tabulated List of Items and Categories from the NIST Workshop along with the Results of this Study Showing the Percentage of Articles Reporting the Respective Items

Category	Item	Articles including item
Absolute dosimetry/ calibration	Published standards used	6.9%
	Detector type used	3.4%
Determination of dose	Published standards used	10.3%
	Specification of media	6.9%
Radiation source specification	Detector type used	27.6%
	Radioisotope	86.2%
	kV, filtration, HVL	50.0%
Irradiation details	Animal/cell type	100%
	Dose details	100%
	Field size and shape	0%
	Geometry of fields	24.1%
	Animal containment	100%

← **12** articles

→ Both reviews were **limited in scope**

Pedersen et al, **Radiation Biology Dose Verification Survey**, Radiation Research 185, 163-168 (2016)

Purpose

- Repeat previous literature review on **much wider** scale
  - **3452** articles from **471** journals published in last **20** years
- For each article, are physics/dosimetric details sufficient to:
  - **Replicate** experiment?
  - **Interpret** results?
  - **Credible** methodology?
- Evaluated following NIST symposium recommendations:
  - Source specification
  - Dose specification
  - Absolute radiation dosimetry calibration
  - Irradiation geometry

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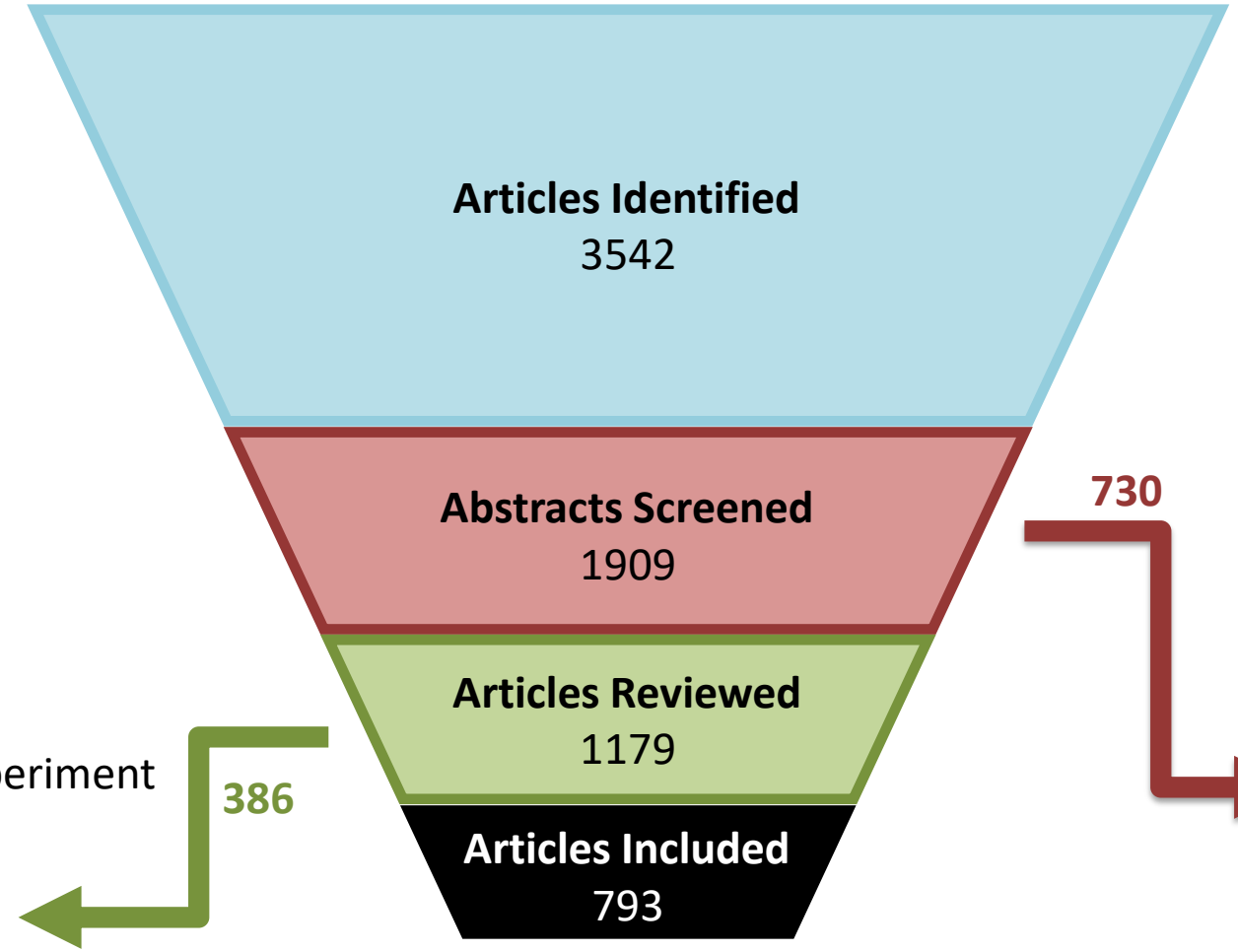
FACTORS IDENTIFIED

- Radiation Source Specification
  - Source type (x-ray, proton, heavy ion, etc…)
  - Beam Quality (Isotope, Energy, HVL)
  - Irradiator Model/Manufacturer
- Absolute Dosimetry\Calibration of the beam
  - Standards used
  - Detector identified
  - Medium for dose specification
  - Calibration geometry (waived when protocol identified)
- Irradiation Details
  - Dose, Dose rate, Fractionation scheme
  - Source geometry (field size, distance, # of fields)
  - Subject geometry (subject size, subject type, backscatter/attenuation)

METHODS – PRISM Analysis



Articles Excluded:

- No ionization radiation experiment (223)
- Imaging (110)
- Not an animal or cell (46)
- Copyright or embargo (7)

Abstracts Excluded:

- Review articles (419)
- Not in English (311)

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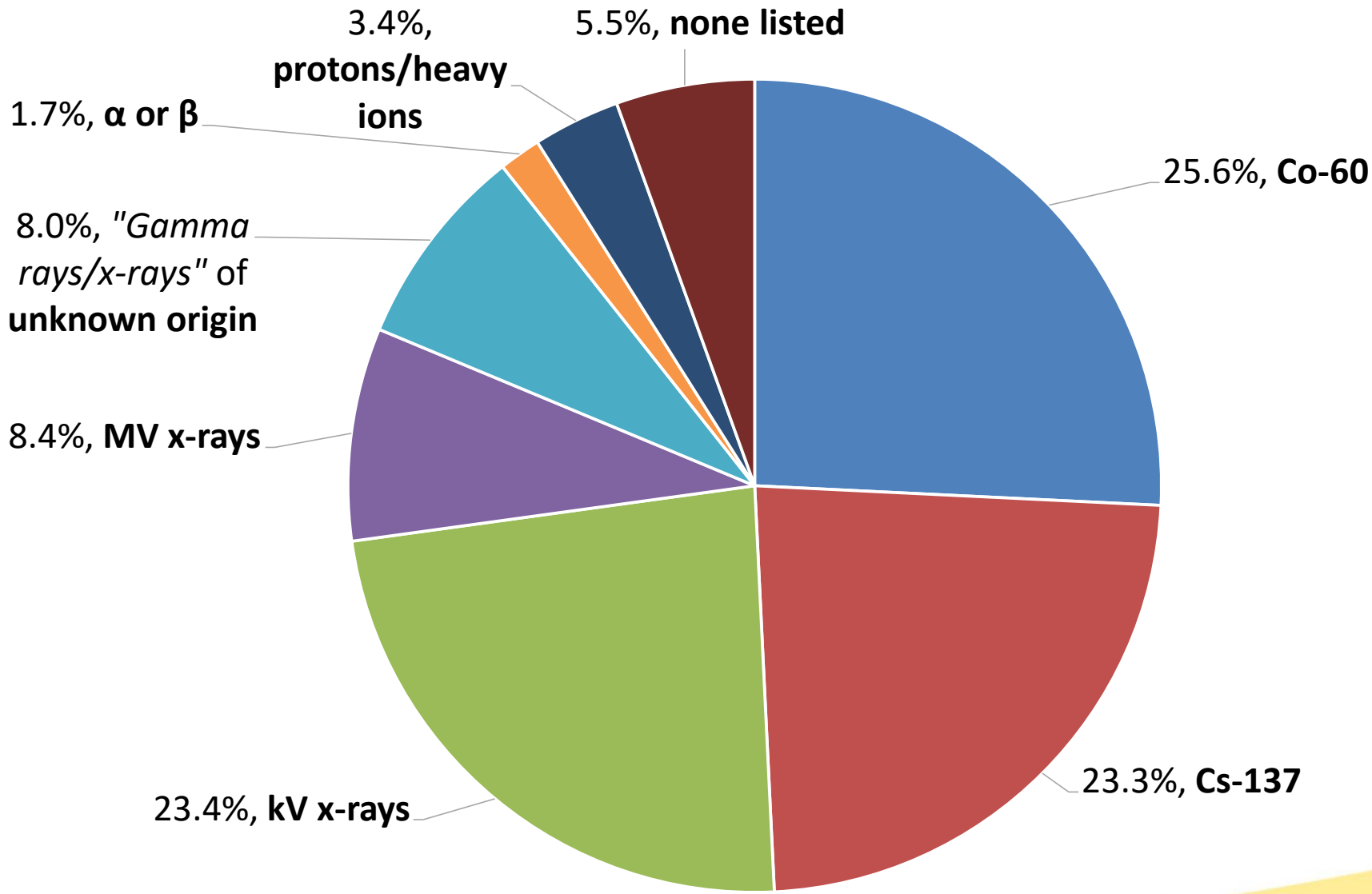
SOURCE TYPES FOR 793 ARTICLES REVIEWED



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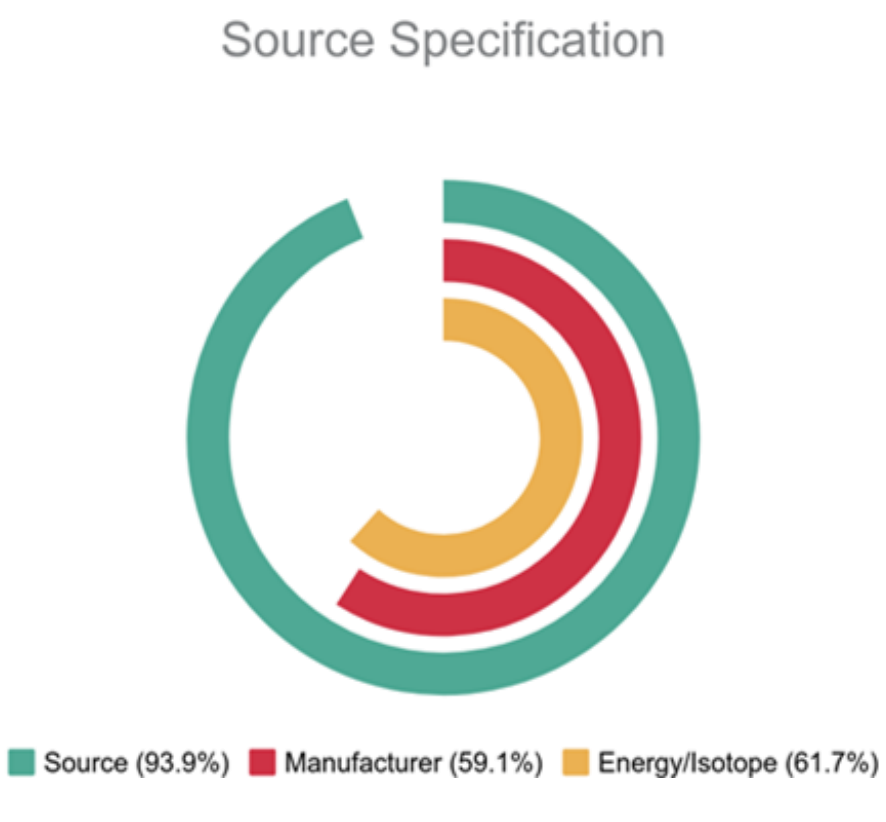
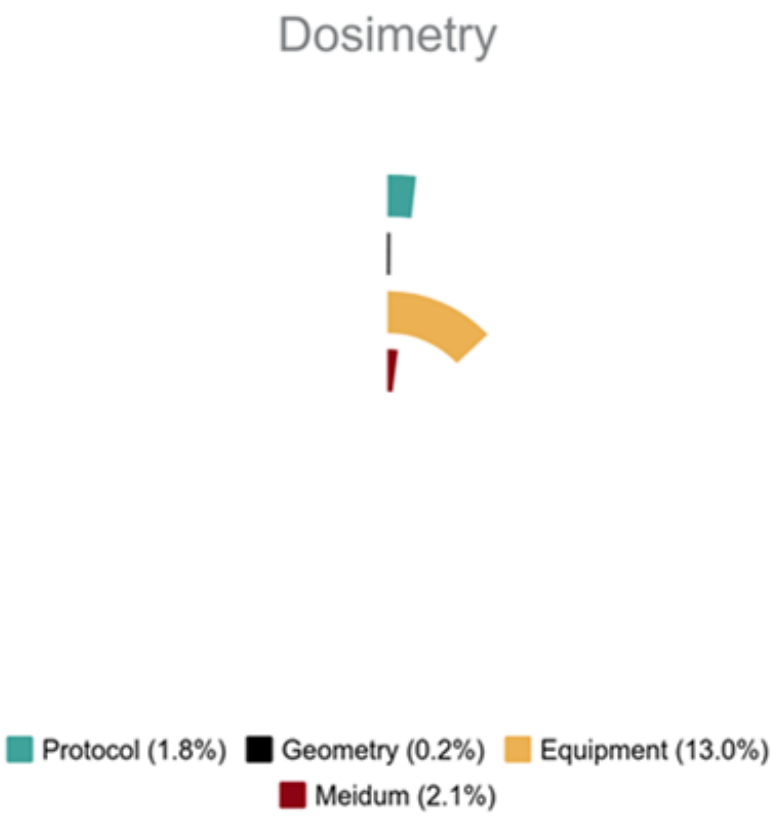
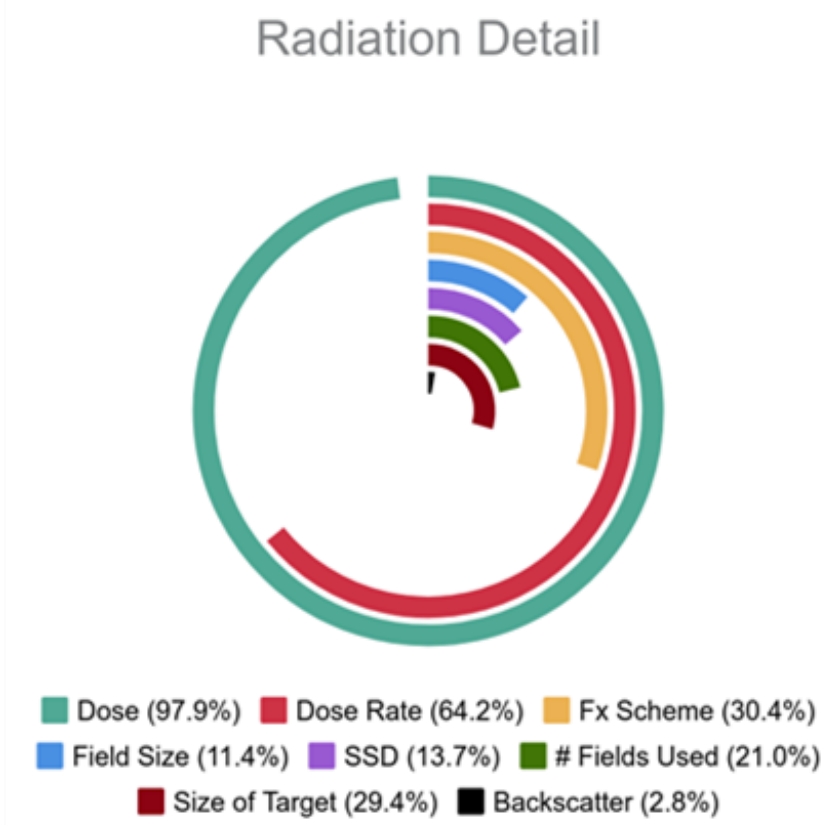
Percentage of articles reporting physics & dosimetry quantities





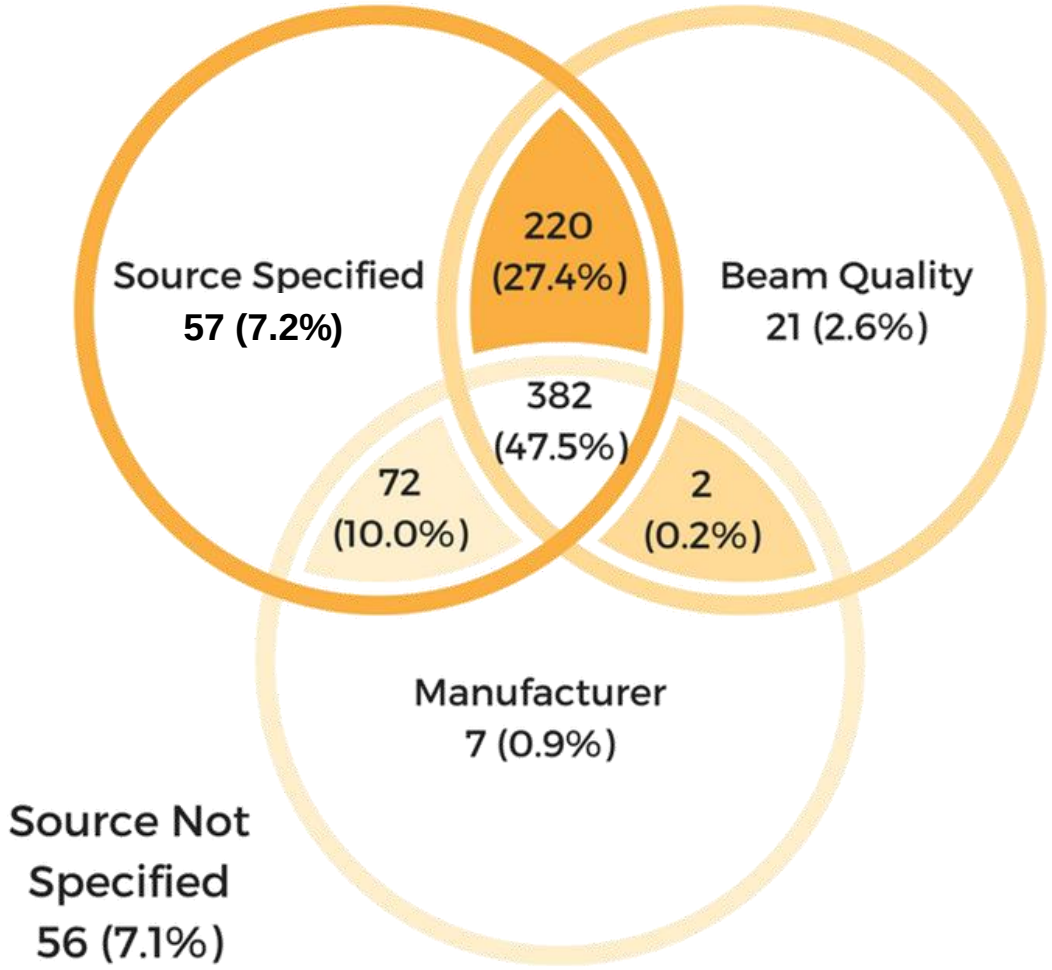


~6% do not report the radiation source
~40% do not report the beam quality

Absolute Calibration is almost entirely **unreported**

Most report the Dose (98%)/Dose rate (64%)
Few report on anything else.

REPORTING FREQUENCY – SOURCE SPECIFICATION



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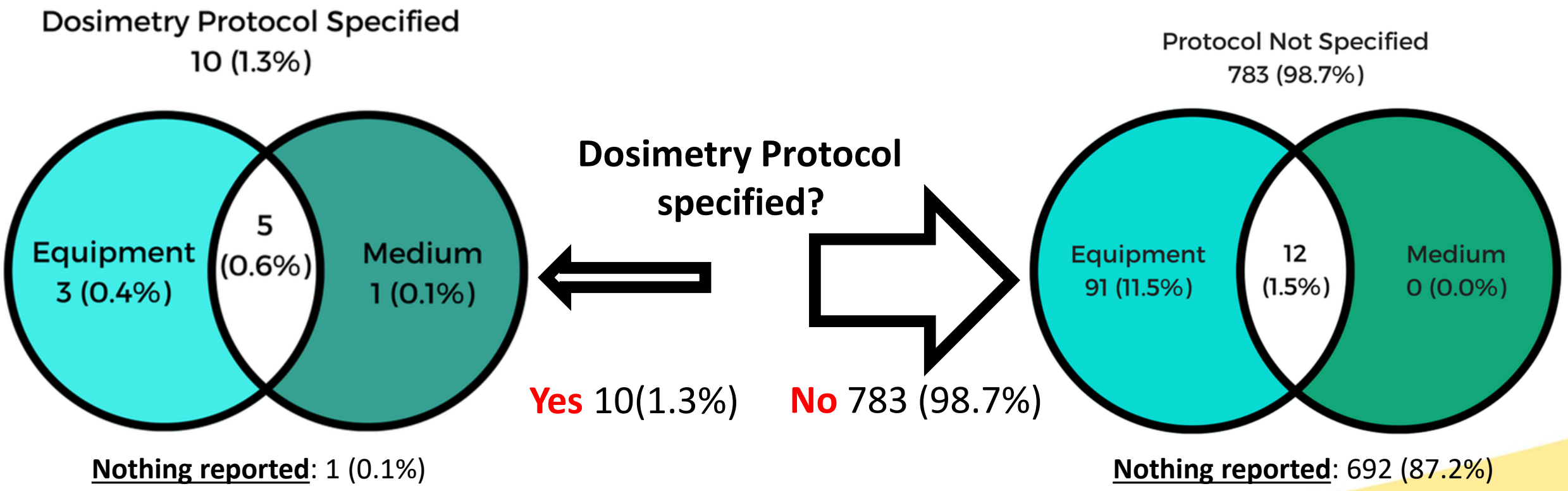
REPORTING FREQUENCY- ABSOLUTE DOSIMETRY



Nothing reported: 1 (0.1%)

Nothing reported: 692 (87.2%)

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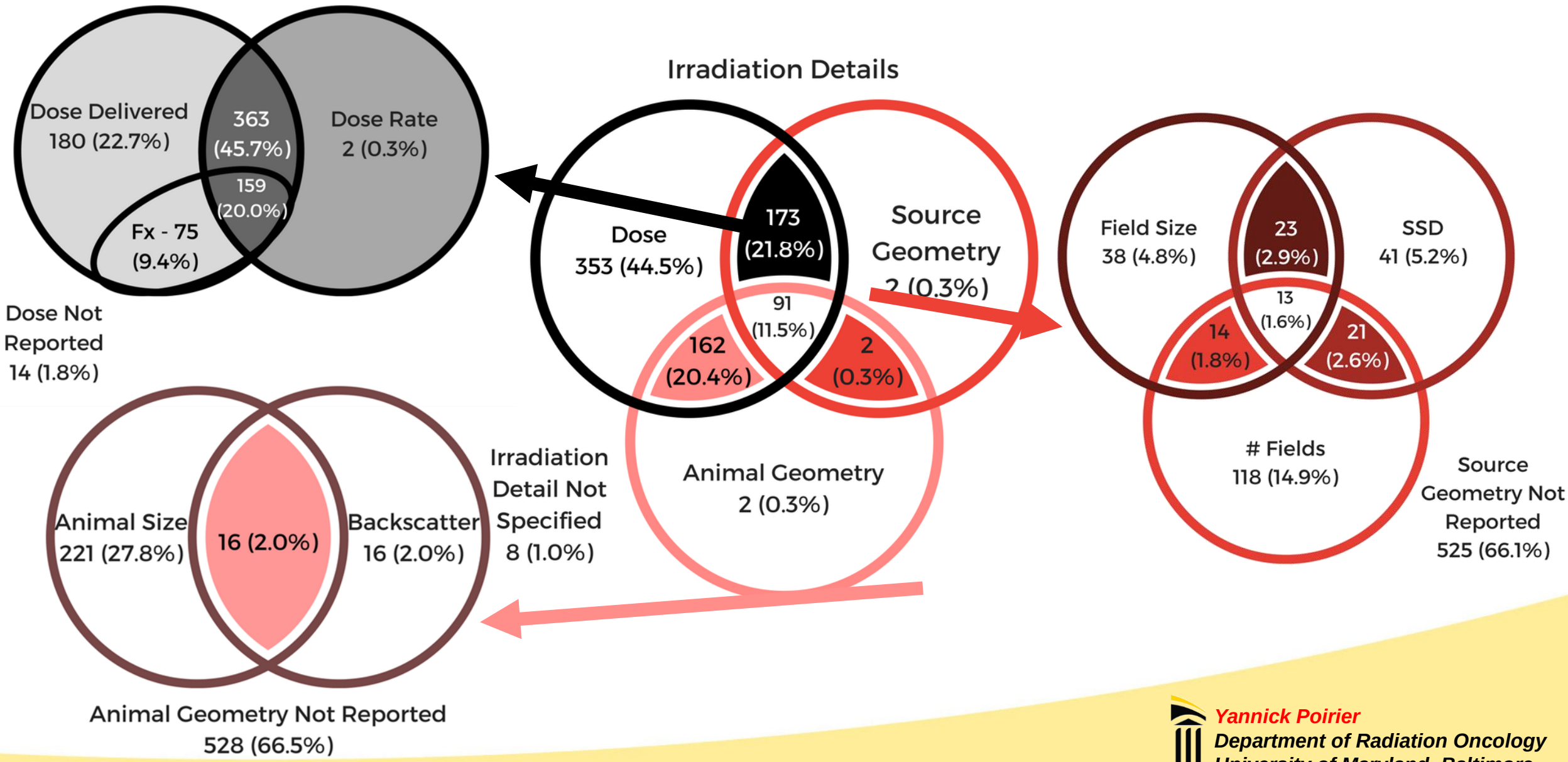
REPORTING FREQUENCY – IRRADIATION DETAILS



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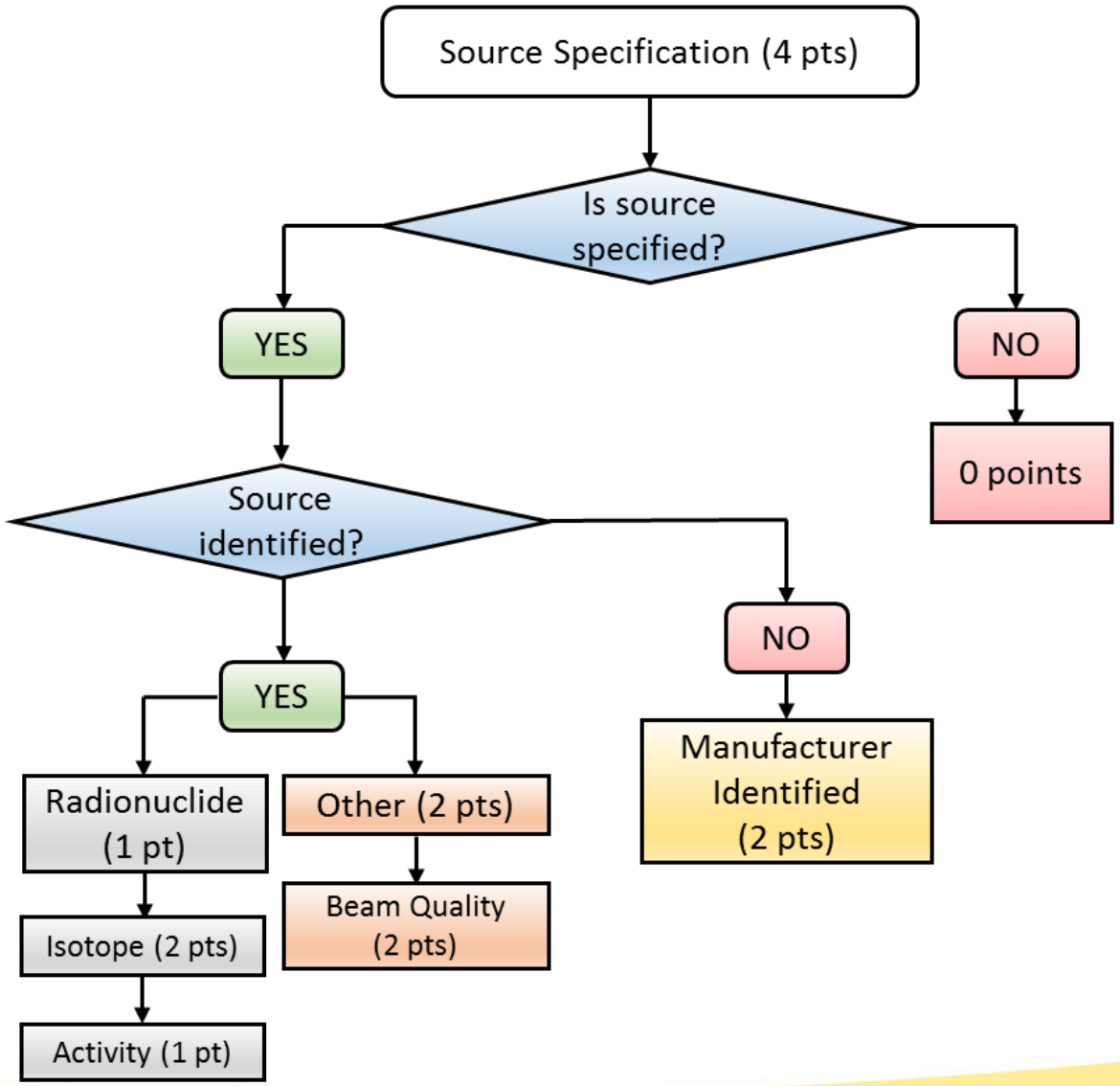
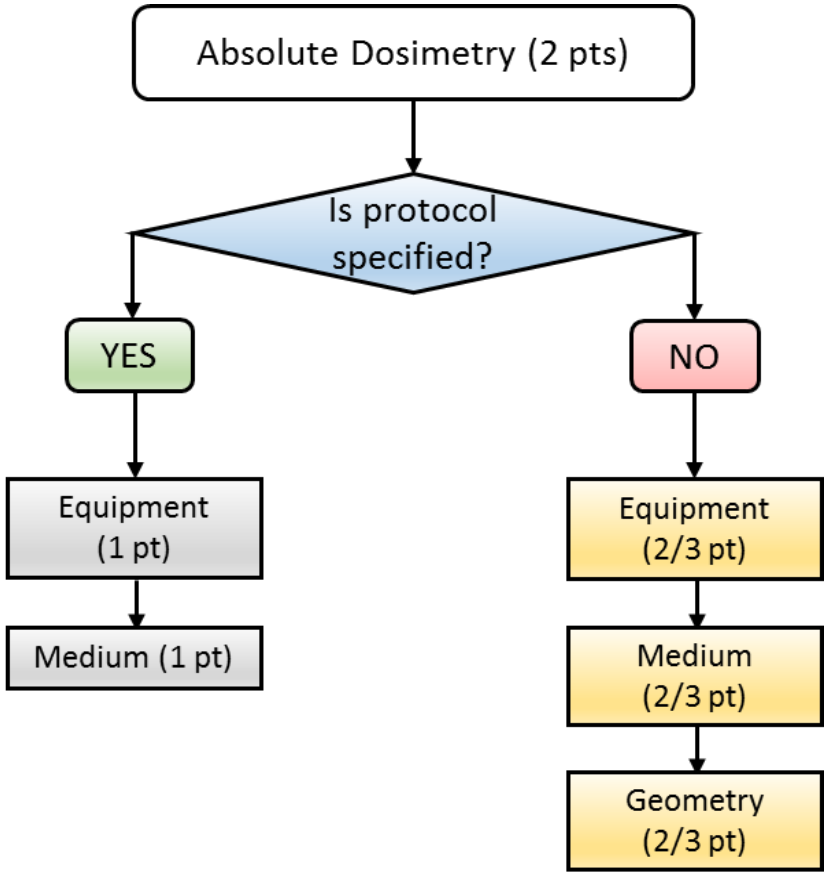
METHODS – Article scoring flowchart





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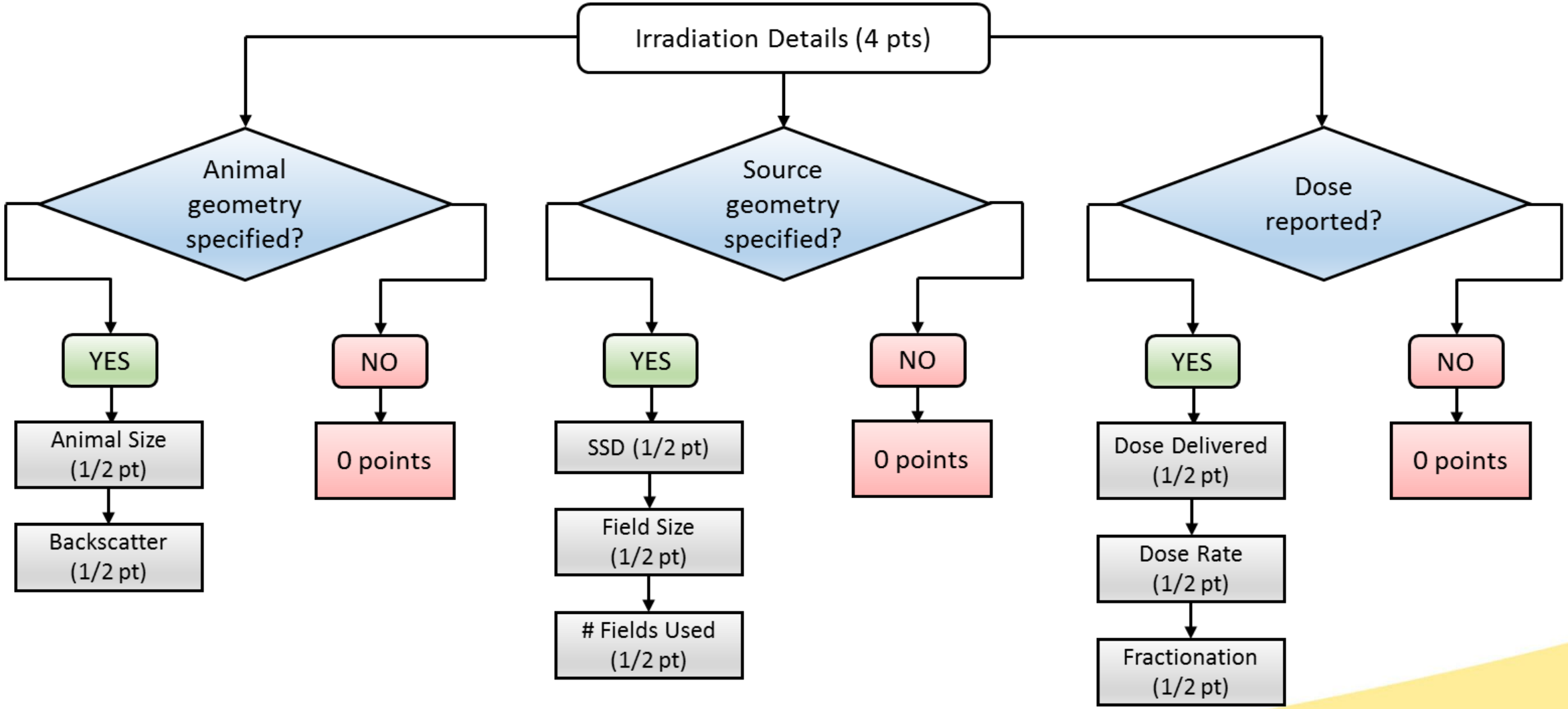
METHODS – Article scoring flowchart



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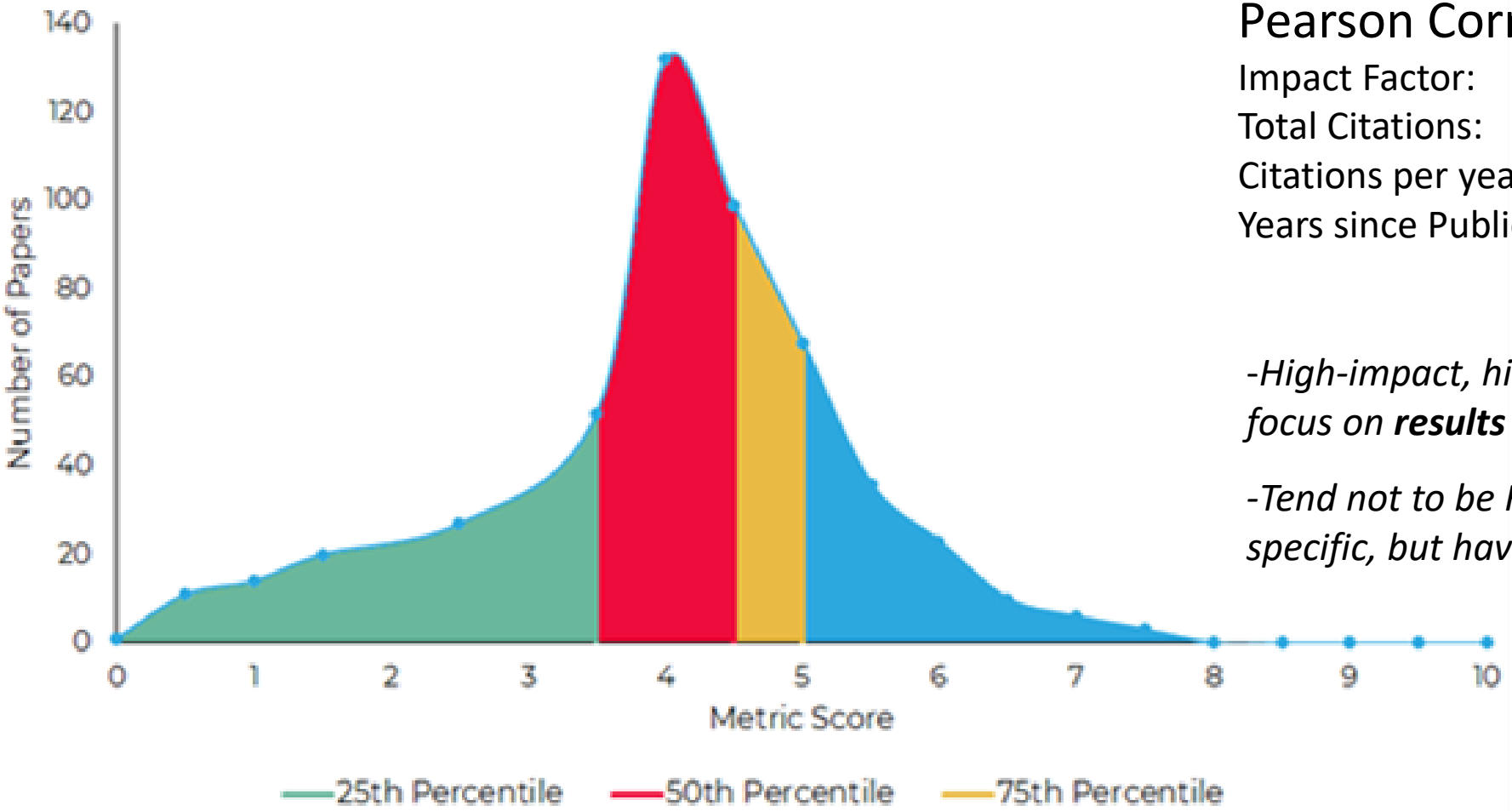
Article Total Score Breakdown



Pearson Correlation Factor

Impact Factor:	-0.23, $p = 6 \cdot 10^{-11}$
Total Citations:	-0.07, $p = 0.03$
Citations per year:	-0.09, $p = 0.009$
Years since Publication:	-0.03, $p = 0.36$

*-High-impact, highly cited journals tend to focus on **results** rather than **methods***

-Tend not to be Radiation Biology/Physics-specific, but have broader audiences

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Where lack of experimental details make interpretation difficult

- Vague description that **can't be interpreted**
  - "Ionizing radiation"
  - "Gamma/x-rays" of *unknown* energy or origin
  - "x-rays delivered from a Siemens x-ray machine"

- Clear errors that don't inspire confidence – impact **credibility**
  - "gamma rays" delivered by X-Rad 320ix **x-ray** irradiator
  - "250 MeV x-ray" from **kV** irradiator
  - "Cs-62" – Is it Cs-137? Co-60? (*Co-62 has 1.5 m half-life*)

- Clearly **impossible** irradiations
  - 150 kV x-rays delivered from TrueBeam MV accelerator

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Conclusion

- First **large scale** (>1000 papers) review of current state of physics & dosimetry reporting in radiation biology at large
- The **majority** report the *subject*, the *dose*, and the source *type*
  - 1.8% do not report **dose**, 5.5% do not report **source**
  - 33% do not report **dose rate**
  - 22% do not report **beam quality**
- Almost none report **dosimetry** or **irradiation geometry**
  - 86% do not report **any dosimetry/calibration** details
  - 66/68% do not report any details on **irradiation/animal geometry**

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Conclusion

- Almost none report on the difference between **calibration** and **animal irradiation** geometry
- Quality of reporting was
  - **Inversely correlated** with **journal impact factor**
  - **Inversely correlated** with **# of citations**, both *total* and *per year*
  - Not correlated with **recentness**
- Currently, the majority of radiation biology articles **do not sufficiently report** experimental details to allow for **interpretation** and **replication**

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Conclusion

- Future work, to investigate:
  - Relationship between **factors reported** and **source type**
  - Articles before vs after **NIST Symposium**
- Unequal access to **physics reviewers**
  - Many “big picture” journals do not
  - Propose “**check sheet**” to more pointedly guide review of physics/dosimetry for non-specialist journals

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