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From the perspective of clinical medical physics in the era of VHEE RT

International Workshop on Very High Energy Electron Radiotherapy 2025

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Schüler Lab Website

“…highlighting any challenges or opportunities you foresee in clinical implementation, particularly in relation to dosimetry, treatment planning, and patient safety.”

"From the perspective of clinical medical physics in the era of VHEE RT" – What is clinical medical physics today?

Radiation Therapy Planning and Optimization

Equipment Commissioning and Quality Assurance

Radiation and Patient Safety

Internal Radiation Therapy

- Nuclear medicine
- Brachytherapy

External Beam Radiation Therapy

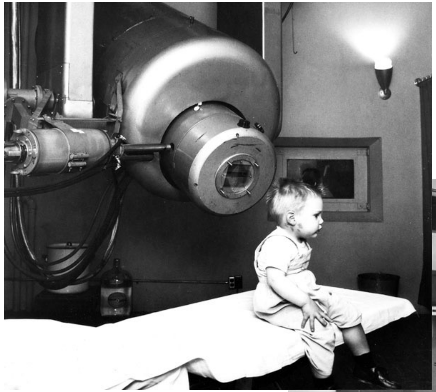
- MV X-rays and Electron RT
- Proton RT

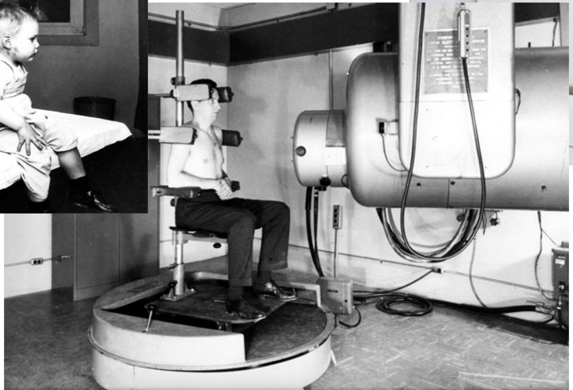
The evolution of modern external beam radiation therapy

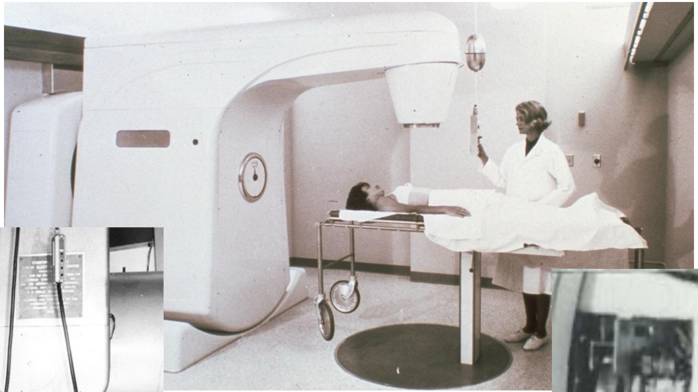
1953 – Dr. Henry Kaplan and physicist Edward Ginzton developed the first medical linear accelerator in the Western hemisphere.

1960 – Varian Clinac ®6/100 introduced, the first fully rotational radiotherapy linear accelerator.

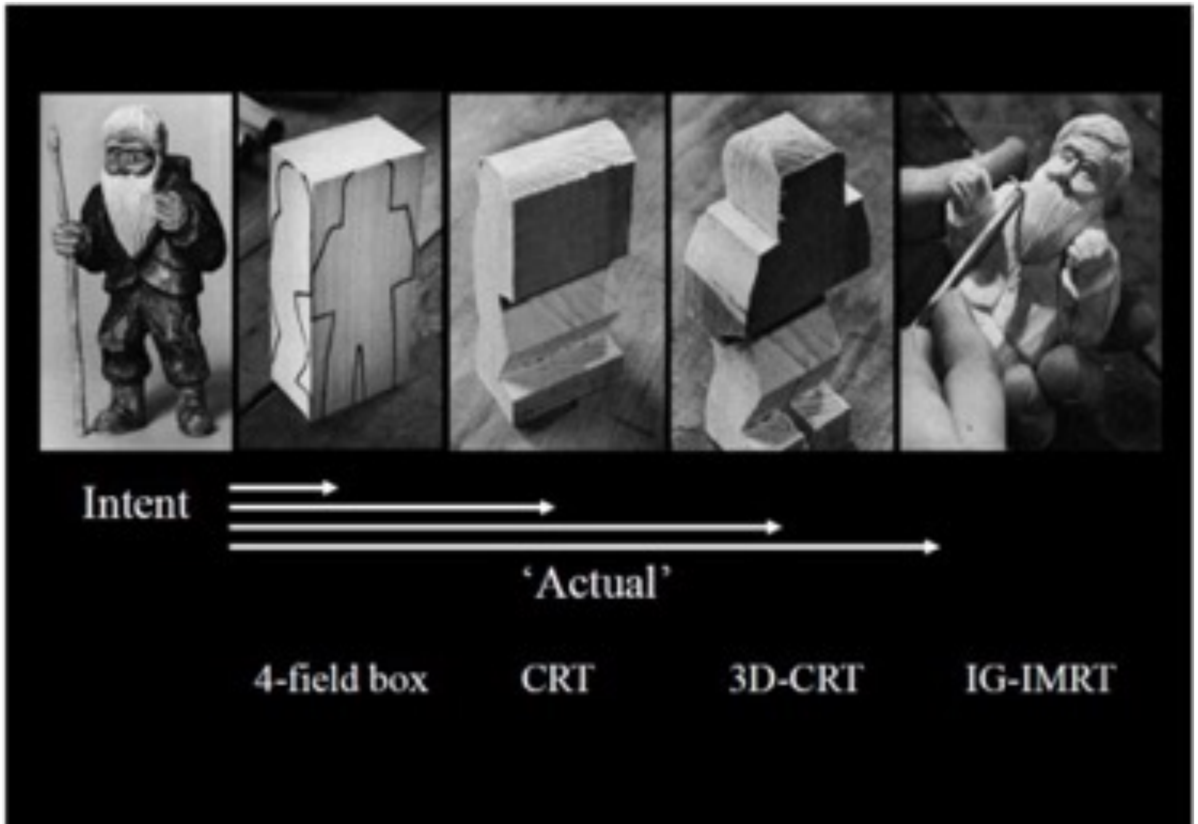
1990 – First hospital-based proton center opened at Loma Linda University Medical Center.

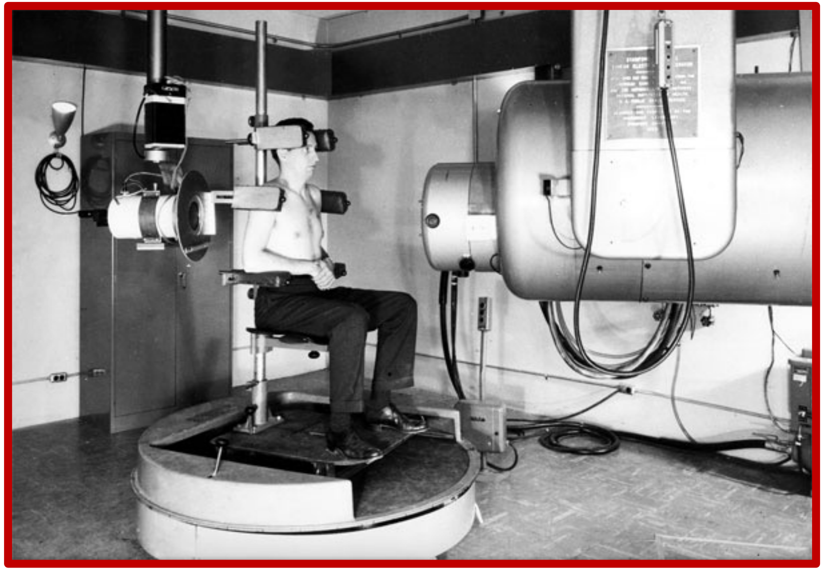






Key developments in RT have stemmed from the desire of increasing dose conformity





Even the desire of increasing dose conformity does not escape the law of diminishing returns

- The incremental improvement from current techniques will likely be small and benefit only the most complex clinical cases

Why VHEE Radiotherapy?

VHEE: very high energy electrons in the range 50-300+ MeV, multiple teams working on developing clinical VHEE machines for RT applications

VHEE RT characteristics:

- Highly penetrating – potential to treat deep-seated tumors with sharp lateral penumbra
- "Easily" manipulated through magnetic components, potentially making VHEE beams highly precise and versatile
- Minimally affected by inhomogeneities

While VHEE has many inherent characteristics that make it highly attractive by itself, its potential for rapid dose delivery coupled with these characteristics makes it the ideal modality for FLASH RT applications

Roadblocks for implementing VHEE RT

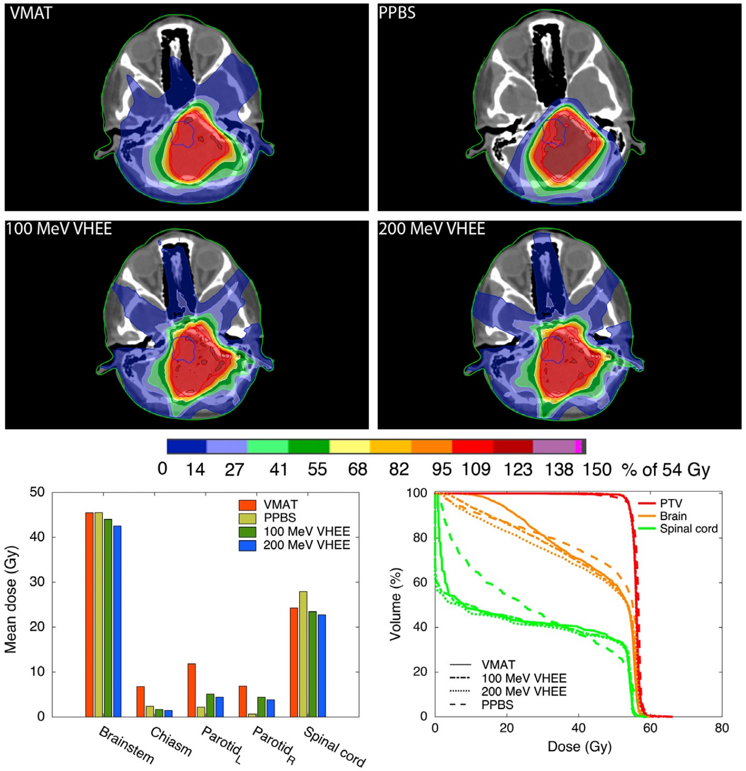
- Technology Readiness
- Biological Uncertainty
- Dosimetry and QA challenges
- Clinical Infrastructure and Shielding
- Cost and Economic Justification
- Clinical Trials and Regulatory Pathways
- Treatment Planning and Imaging Integration

Where would VHEE RT “live” within our current RT framework?

Is VHEE RT another modality to choose from, or is it a “disrupter” that will become paradigm-shifting?

Schueler *et al.* Med Phys 2017

VHEE is superior to MV X-ray in the majority of cases



VMAT				PPBS				100 MeV VHEE				200 MeV VHEE			
$\bar{D}_{Body}(Gy)$	CI_{100}	CI_{50}	HI	$\bar{D}_{Body}(Gy)$	CI_{100}	CI_{50}	HI	$\bar{D}_{Body}(Gy)$	CI_{100}	CI_{50}	HI	$\bar{D}_{Body}(Gy)$	CI_{100}	CI_{50}	HI
6.3	1.02	3.54	0.093	5.0	1.17	4.21	0.14	6.3	1.05	3.63	0.093	6.1	1.04	3.45	0.086

$CI_{100} = V_{100\%}/V_{PTV}$ $CI_{50} = V_{50\%}/V_{PTV}$ HI = (D2-D98)/D50

Schueler *et al.* Med Phys 2017

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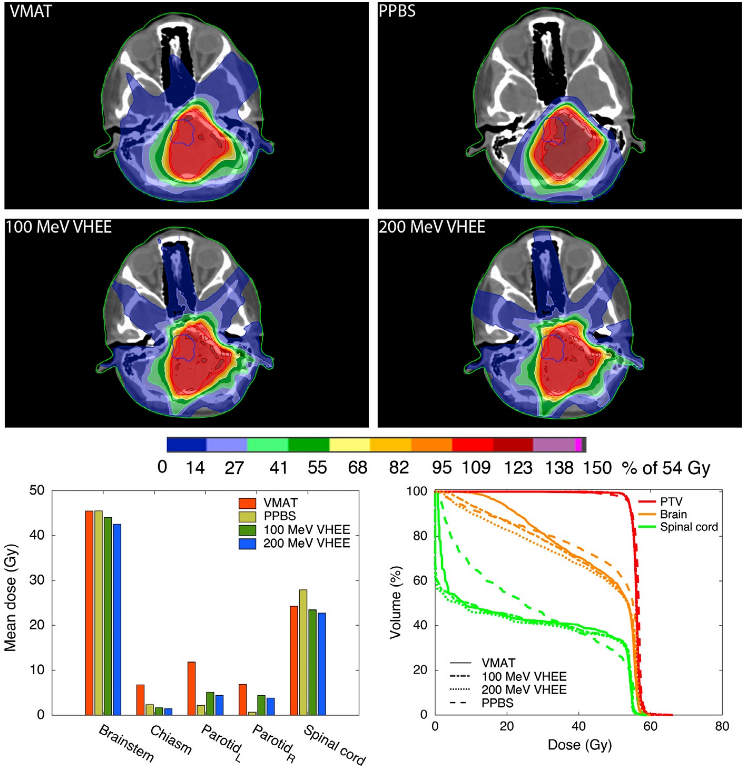

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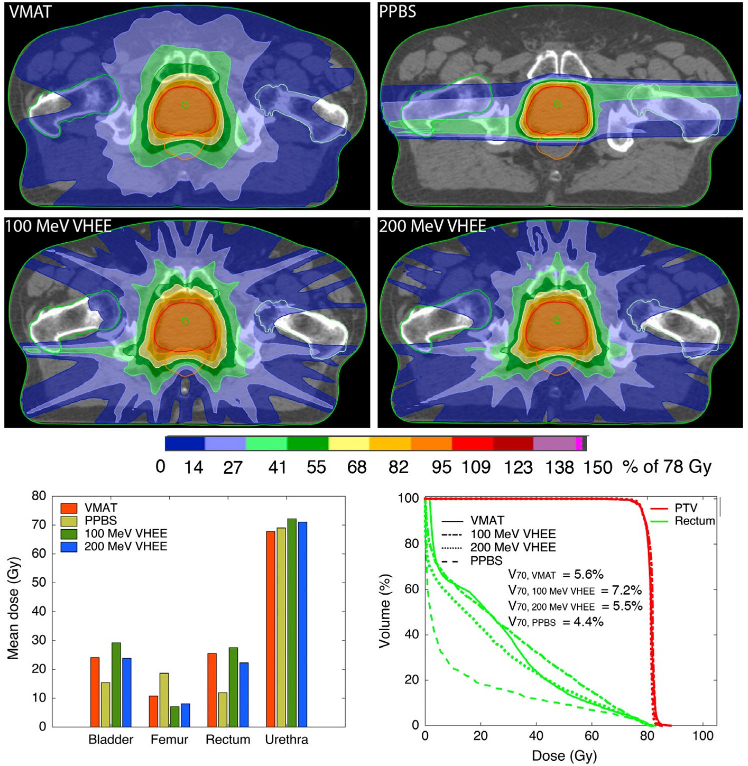

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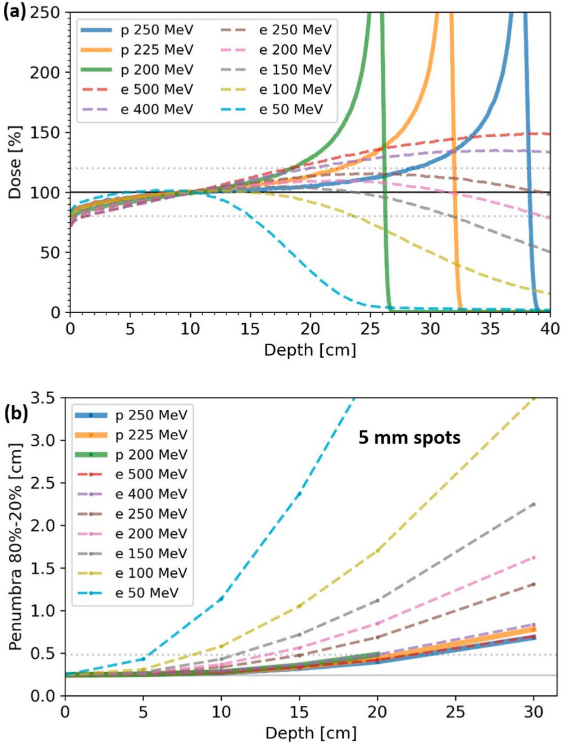
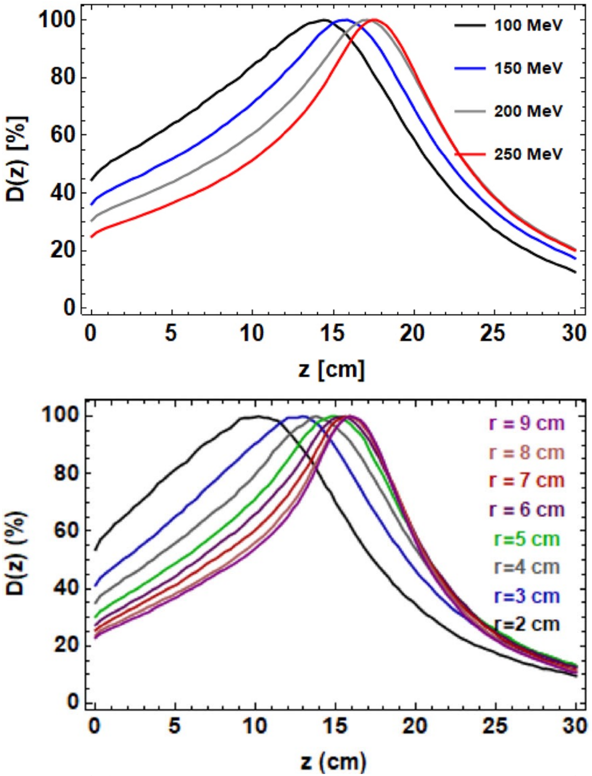
4.4	1.00	3.45	0.090	2.1	1.02	2.41	0.083	4.1	1.10	4.27	0.093	3.9	1.06	3.48	0.071

$CI_{100} = V_{100\%}/V_{PTV}$ $CI_{50} = V_{50\%}/V_{PTV}$ HI = (D2-D98)/D50

VHEE can offer unprecedented precision and flexibility!



Böhlen *et al.* Radiotherapy and Oncology 2024



Whitmore *et al.* Sci. Rep. 2021 and 2024

Equipment Commissioning and Quality Assurance

- Dosimetry

Equipment Commissioning and Quality Assurance

- Dosimetry

What can we expect from a clinical VHEE RT unit?

Dosimeters and their capabilities rated for potential FLASH dose measurements

TABLE 1 | Dosimeters and their capabilities rated for potential FLASH dose measurement of key parameters.

Response	Detectors	Measurement type	FLASH study	Instantaneous dose-rate/dose per pulse (D_p) dependence	Spatial resolution	Time-resolution	Energy dependence
Luminescence	TLD/OSLD	**1D**, 2D	e [15, 37, 71]	Independent (~10^9 Gy/s) [80, 137]	~ 1 mm	Passive	Tissue-equivalent
	Scintillators	1D, **2D**, 3D	p [13, 18]	Independent (~10^6 Gy/s) [29]	~ 1 mm	~ns	Tissue-equivalent
	Cherenkov	**1D**, 2D, 3D	e [29]	Independent (~10^6 Gy/s) [29]	~ 1 mm	~ps	Energy dependent
	FNTD	2D	NA	Independent (~10^8 Gy/s) [85]	~ 1 µm	Passive	Energy dependent
Charge	Ionization chambers	**1D, 2D**	p [13, 18, 19] e [15, 37, 71] ph [16, 17]	Dependent on D_p [48, 52] (>1 Gy/pulse),	~3–5 mm	~ms	Energy dependence shows up > 2 MeV
	Diamonds	**1D**	p [18]	Dependent on D_p (>1 mGy/pulse) [49]	~ 1 mm	~µs	Tissue-equivalent
	Si diode	**1D**, 2D	NA	Dependent on D_p [54] (Independent ~0.2 Gy/s) [138]	~ 1 mm	~ms	Energy dependent
Chemical	Alanine pellets	**1D**	e [12, 15, 37, 139]	Independent (10^8 Gy/s) [69]	~ 5 mm	Passive	Tissue-equivalent
	Methyl viologen/fricke	**1D**	e [29, 48]	Depends on the decay rate and diffusion of radiation induced species	~ 2 mm	~ns	Tissue-equivalent
	Radiochromic film	**2D**	p [18, 19] e [10–12, 15, 30, 37, 71, 140] ph [16]	Independent (10^9 Gy/s) [70, 71]	~1 µm	Passive	Tissue-equivalent
	Gel dosimeters	3D	NA	Strong dependence below 0.001 Gy/s [141] and above 0.10 Gy/s [142]	~1 mm	Passive	Tissue-equivalent

Ashraf *et al.* Frontiers in Physics 2020

Dosimeters and their capabilities rated for potential FLASH dose measurements

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Lumin[illegible]	TLD/OSLD	**1D**, 2D	e [15, 37, 71]	Independent (~10[illegible]) [illegible]0, 137]	~ 1 mm	Pa[illegible]	Tissue-equivalent
	Scintillators	1D, **2D**, 3D	p [13, 18]	Independent (~10[illegible]s) [29]	~ 1 mm	~ns	Tissue-equivalent
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Chem[illegible]	Alanine pellets	**1D**	[illegible], 15, 37, 139]	Independent (1[illegible]) [illegible]]	~ 5 mm	Pas[illegible]	Tissue-equivalent
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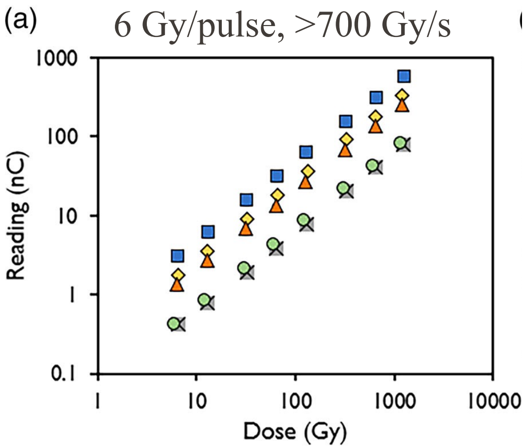
Ashraf *et al.* Frontiers in Physics 2020

Ion chambers

- Advanced Markus
- Exradin A10
- Exradin A26
- Exradin A20
- Exradin A20 (modified)



Liu *et al.* Med Phys 2024

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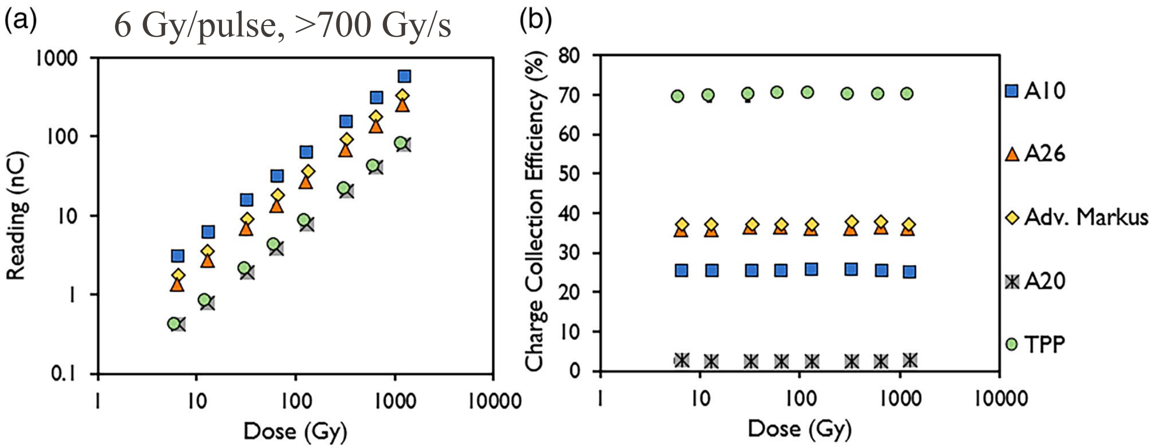

Liu *et al.* Med Phys 2024

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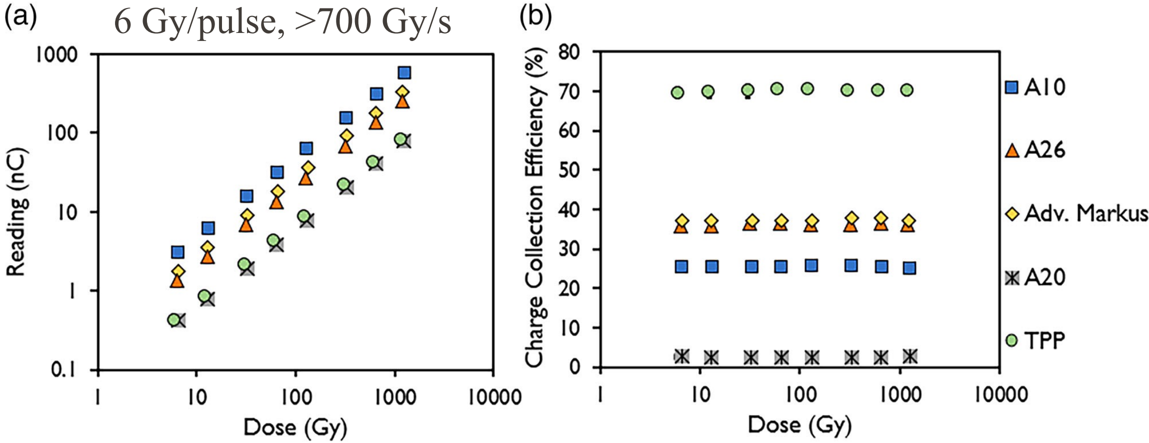
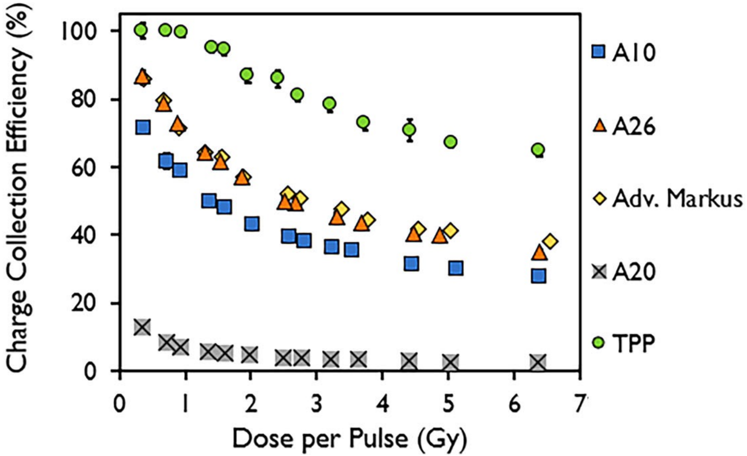
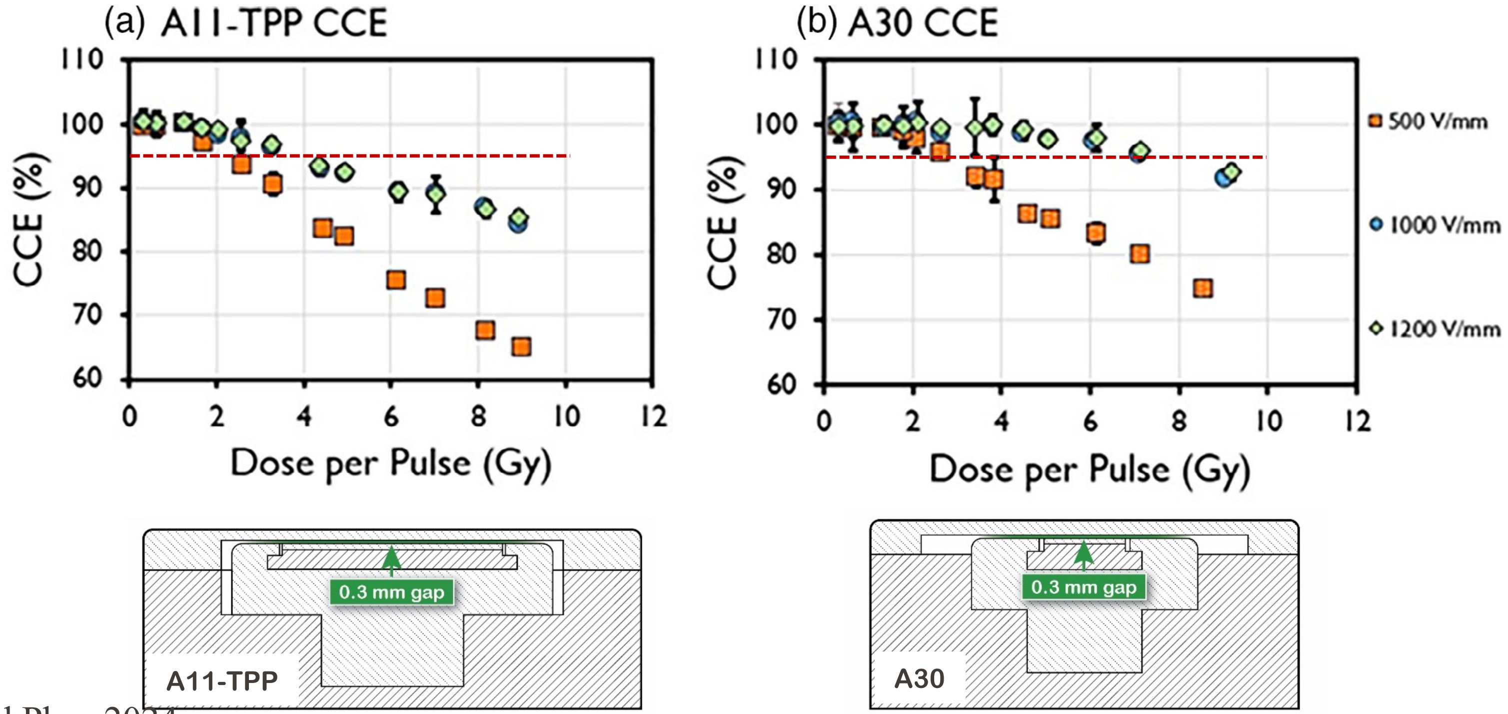




Liu *et al.* Med Phys 2024

New ion chambers have been developed that can serve as reference class chambers for calibration purposes



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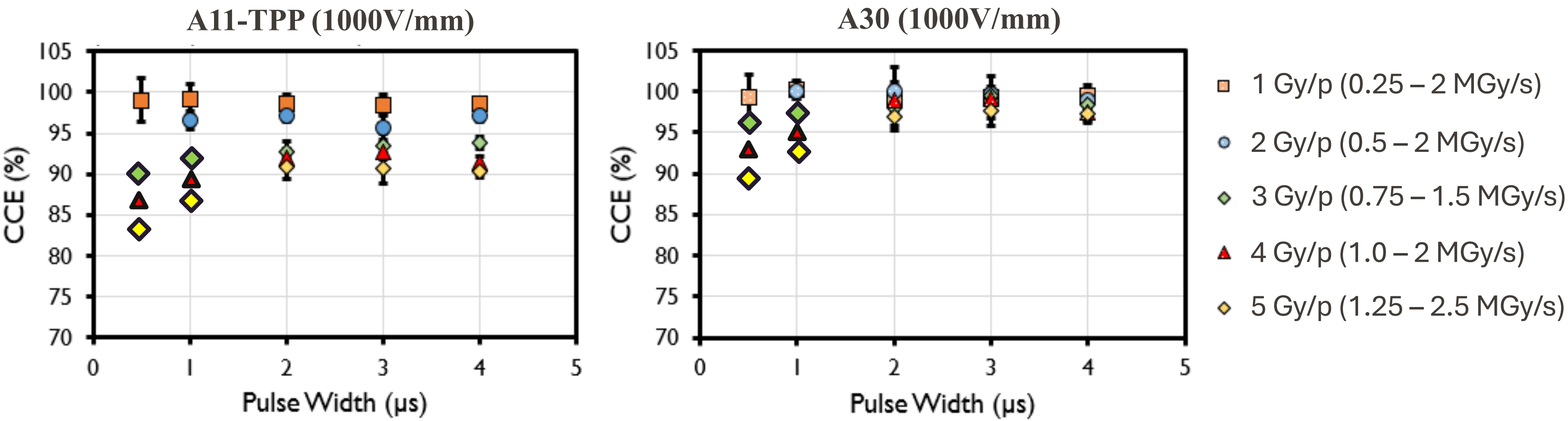
The charge collection efficiency of ion chambers is dependent on dose per pulse and instantaneous dose rate



Liu *et al.* Med Phys 2024

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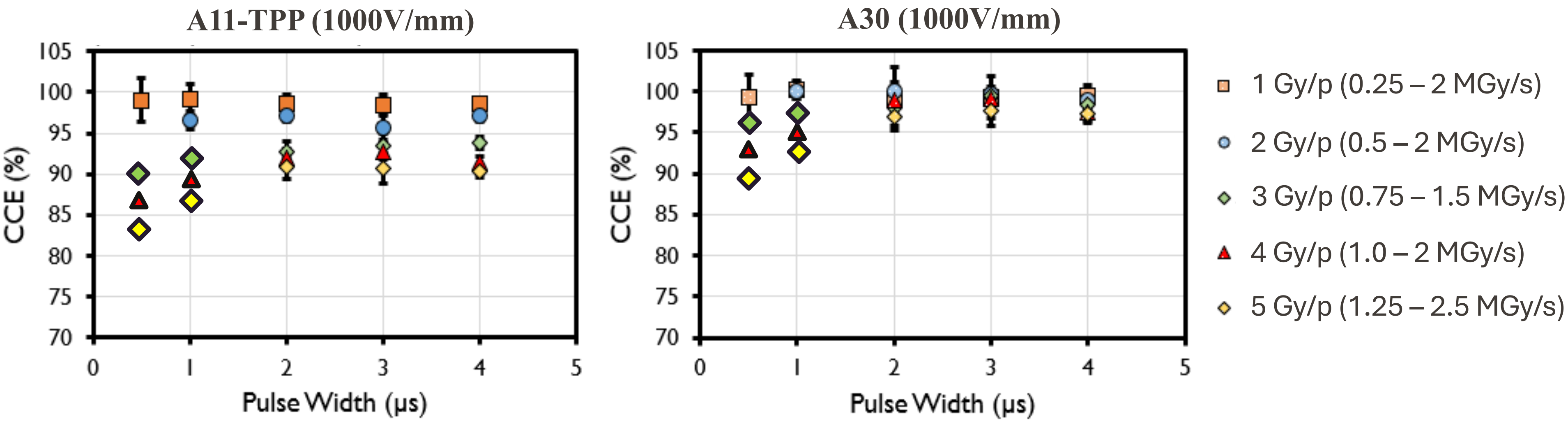

With increasing instantaneous (intra-pulse) dose rate, the dose per pulse that still allows >95% charge collection efficiency goes down

Liu *et al.* Med Phys 2024

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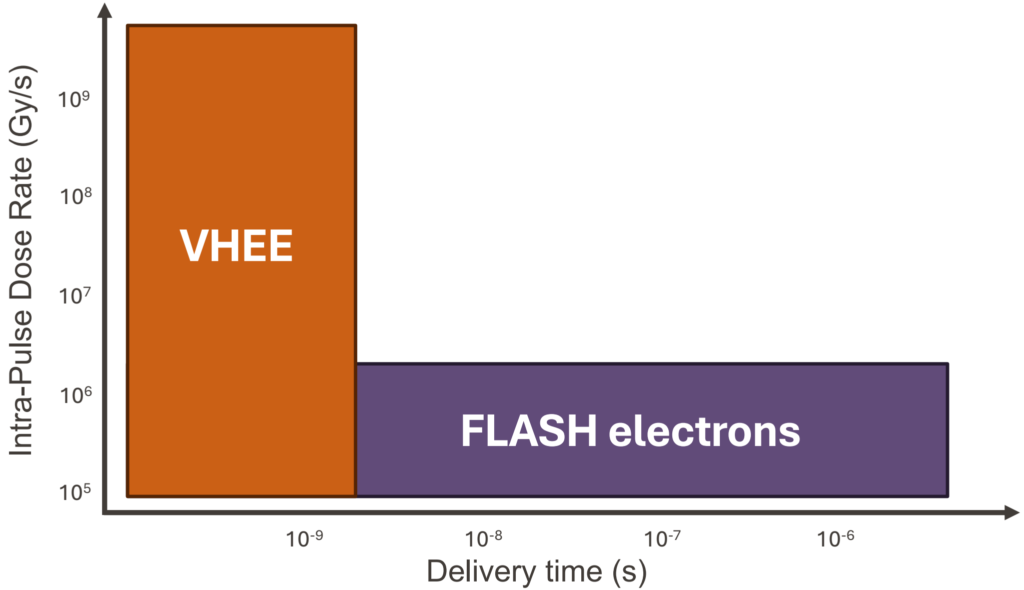

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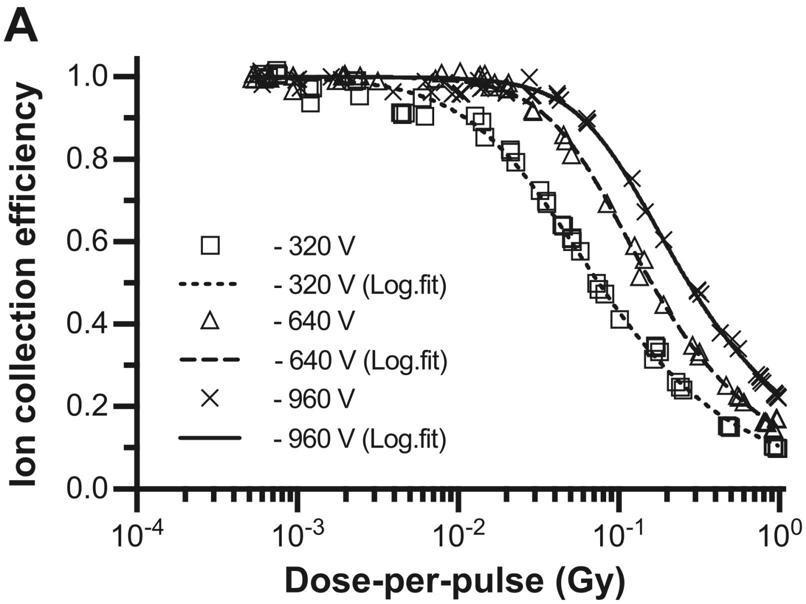
How about beam monitoring and control

Ion recombination effects in traditional transmission ion chambers limits their use in UHDR beams



Limitations of ion chambers

- Slow ion collection time (10 to >100 μs)
  - Limited to dose per pulse measurements if readout electronics can be made fast enough
- High degree of saturation
  - Can be corrected for using empirical models

Konradsson *et al.* Rad Res 2020

As far as possible, compliance to established protocols and guidelines for EBRT should be maintained

	Target / Tolerance
Beam Output Constancy	±2% daily
Beam Energy Constancy (photon/electron)	±2% or ±2 mm depth dose
Range verification (protons)	±1 MeV or ±1 mm range
Dose Rate Accuracy	±2%
Beam Position Accuracy (protons)	±1mm
Radiation Leakage	<0.1% at 1 m

(Reports from IEC 60601, AAPM, NRC)

Criteria for reportable medical event (NRC)

- Total dose differs by ≥20% from the prescribed dose.
- Single fraction dose differs by ≥50% from the prescribed dose.
- Use of the wrong treatment modality or energy.

As far as possible, compliance to established protocols and guidelines for EBRT should be maintained

The IEC 60601-2-1 standard requires that:

- At least two independent dose monitoring systems must be present. These systems must:
  - Continuously measure the radiation dose during treatment.
  - Be capable of automatically terminating the beam if the measured dose exceeds the prescribed value or if a fault is detected.
    - If primary dose monitoring system fails, secondary terminates the beam after 5-10% additional dose.

Underlying principle is that the dose delivered to the patient is within 5% of the prescribed dose (including all uncertainties). Thus, measurement uncertainty should be kept below 1%

Roadblocks for implementing VHEE RT

- Technology Readiness
- Biological Uncertainty
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- Treatment Planning and Imaging Integration