A State-of-the-Art Deep Learning Approach to Proton Dose Reconstruction from PET Activity Measurements

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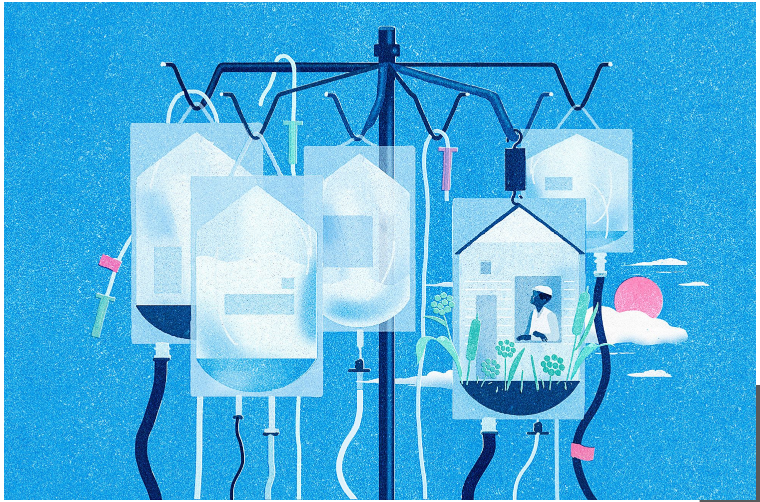
Introduction: What is cancer and how do we treat it?

- Cancer is the **leading** cause of death (1 in 6) worldwide
- Treatment techniques:
  - **Surgery**
  - **Chemotherapy**
  - **Immunotherapy**
  - **Radiotherapy (> 50% of patients)**:

    Last few decades, a new technique grows to precisely target tumors

→ **Proton Therapy**



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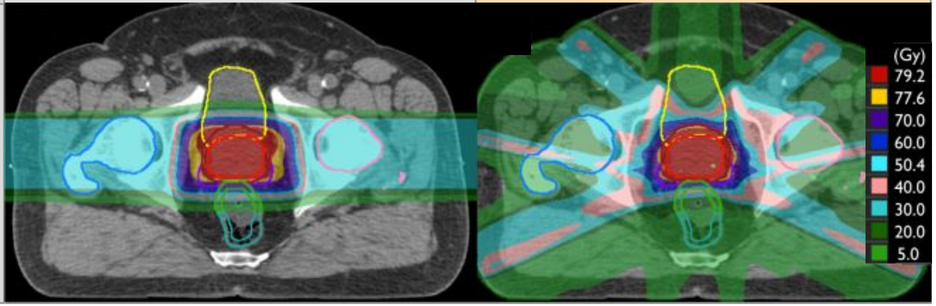
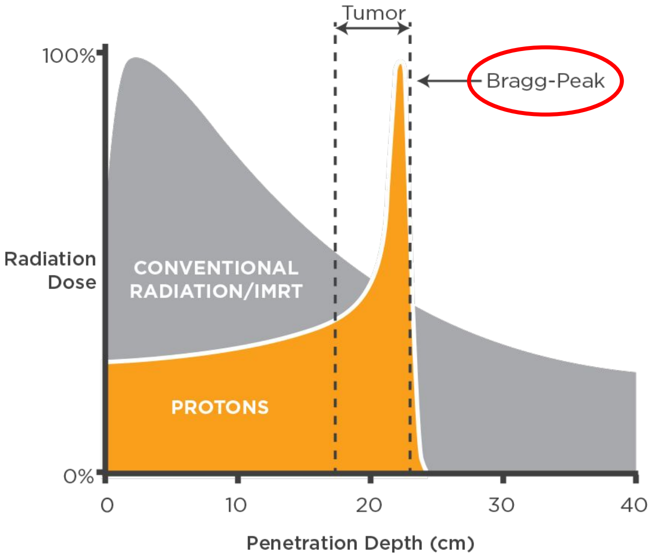
Introduction: What is Proton Therapy?

	Conventional Radiotherapy	Proton Therapy
Objective	Damage DNA of cancer cells to eliminate the tumor	
Radiation Type	High-energy X-rays **(photons)**	**Protons**
Dose Deposition	Peak after entering the body	**Bragg Peak** at specific depth, sharp drop off
Sample Prostate Dose Distribution Kamran et al. 2019		



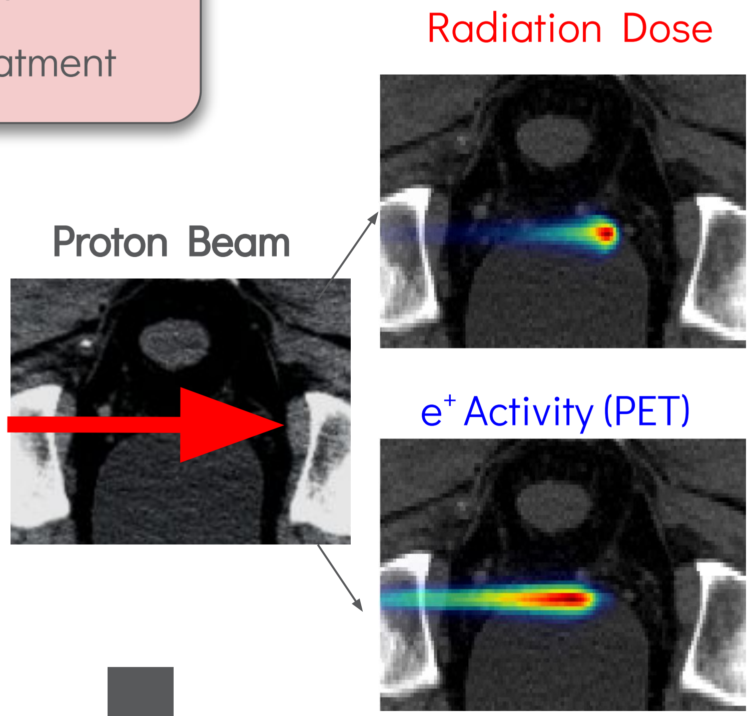
Desouky et al. 2015

Introduction: Challenges of Proton Therapy

- Dose deviations -positioning, physiological changes-
  - ↳ Damage to healthy organs / Tumour undertreatment

↓ Need to verify dose deposition

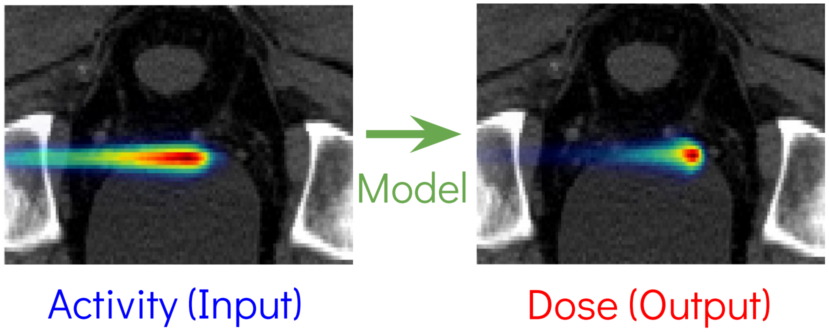
- Proton beams induce e^+ activity ➜ **PET**
- **If the relationship between activity and dose is understood, dose deviations can be detected, enabling** adjustments between sessions



Introduction: Predicting Dose from Activity

- **How?**

  1. Monte Carlo simulations
  2. Activity-Dose Image Pairs
  3. Models to predict dose (output) from PET measured activity (input)



- **Current approaches:**
  - Linear Combinations of Beams[1] (fast, limited)
  - Deep Learning (RNNs[2,3] -1D, unscalable-, or GANs[4,5,6] -outdated-)

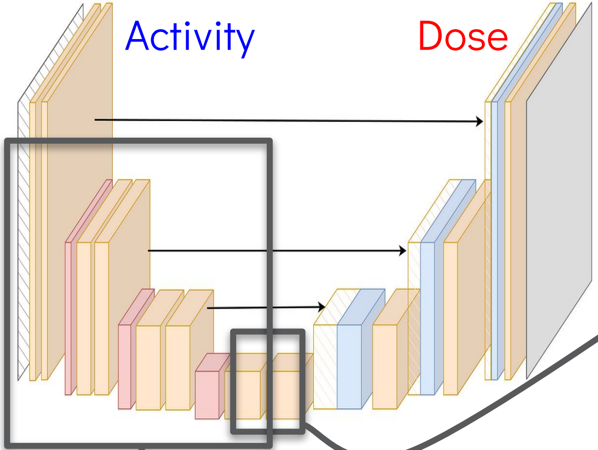
We propose: **State-of-the-Art Vision Transformer Models trained with goal-oriented metrics**

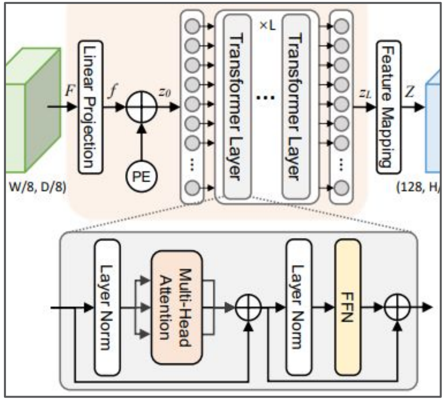
1 Onecha et al. 2021
2 Li et al. 2019
3 Liu et al. 2019
4 Rahman et al. 2022
5 Ma et al. 2020
6 Zhang et al. 2021

Method: The Neural Networks

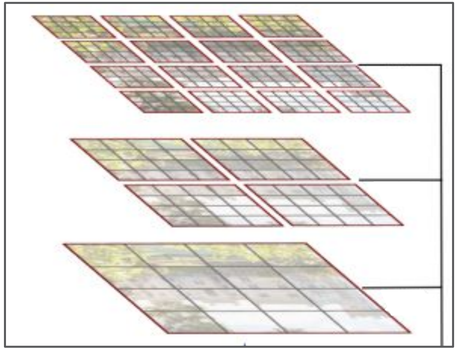
- **Transformers** leverage **attention** to understand the relation between parts of the image
- Input: Activity **or** CT + Activity

Vanilla U-Net	TransBTS	SwinUNETR
Reference; Three	Transformer in bottleneck	Transformer applied on **S**liding **win**dows at different resolutions





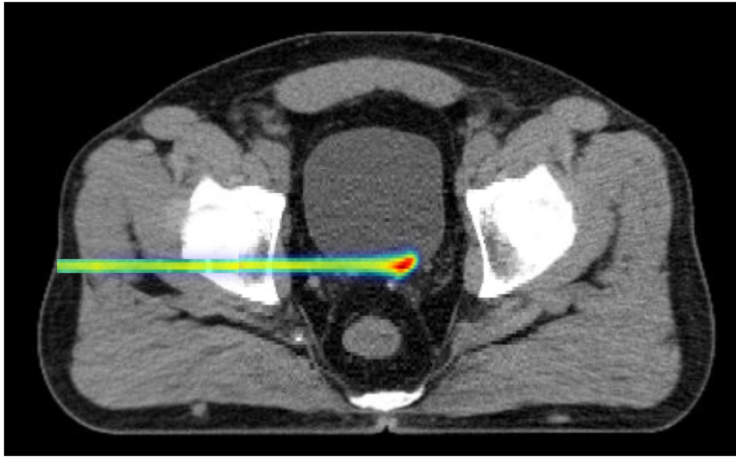
Wang et al 2021



Hatamizadeh *et al* 2022

Method: Dictionary Generation and Metrics

- Simulation of **prostate** treatment plan:
  - Dictionary generation time ~2 hours *(TOPAS)* on CT obtained ~24h prior to treatment
  - 10^5 histories/beam (124 -194 MeV)
  - Dictionary size ~5 GB (1x2x2 mm resolution)
- **Metrics**:
  - Training and Testing:
    - Mean Squared Error
    - Differentiable Gamma Index (DTA = 1 mm, Δ = 3%)[1]
  - Only Testing:
    - Mean Relative Error
    - Gamma Index
    - Bragg Peak Deviation



Passing criteria: $\Gamma(P_r) \leq 1$

DTA (Distance-To-Agreement) = 1mm

Δ = Relative Dose Difference Tolerance = 3%

[1]Martinot et al. 2023

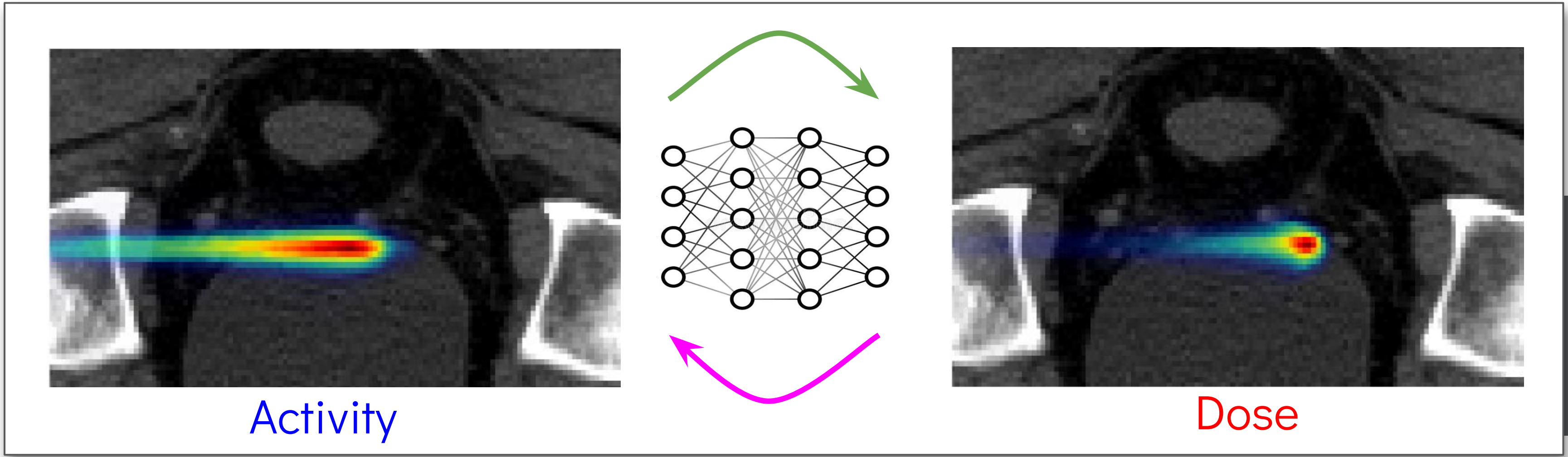
Method: A novel method for out-of-distribution sample detection

Neural Networks may fail with cases outside of their training data distribution

↳ It is important to be able to identify **out-of-distribution (OOD)** samples

PROPOSED METHOD: Train both the **direct** & **reverse** models: Dose (Input) to Activity (Output)

The iterative application of both models will deviate from the original case if sample is **OOD**



Results: Model Performance

(In bold, the best result)

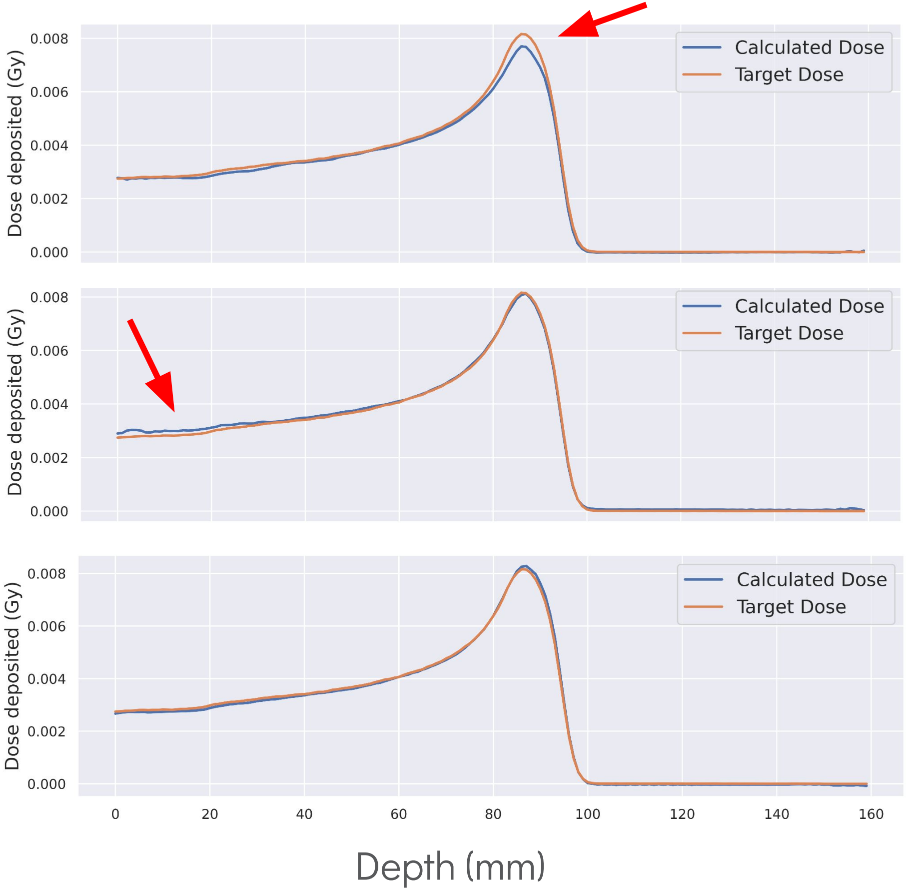
	Vanilla U-Net	TransBTS	SwinUNETR	SwinUNETR w/ CT	SwinUNETR w/ Gamma Loss
Mean Squared Error [%]	0.25	0.17	0.13	0.15	**0.10**
Mean Relative Error [%]	0.024	0.026	0.021	0.027	**0.021**
Bragg Peak Deviation [mm]	0.65	0.60	0.56	0.59	**0.55**
Diff. Gamma Index (1mm, 3%) [%]	97.07	97.86	98.30	98.50	**98.57**
Gamma Index (1mm, 3%) [%]	99.40	99.80	**99.99**	99.98	99.95
Training Time [s] 50 epochs w/ NVidia GeForce RTX 2080Ti	**1h 38min**	2h42min	2h36min	3h2min	2h41min
Output Generation Time [s]	**< 0.1 s**				

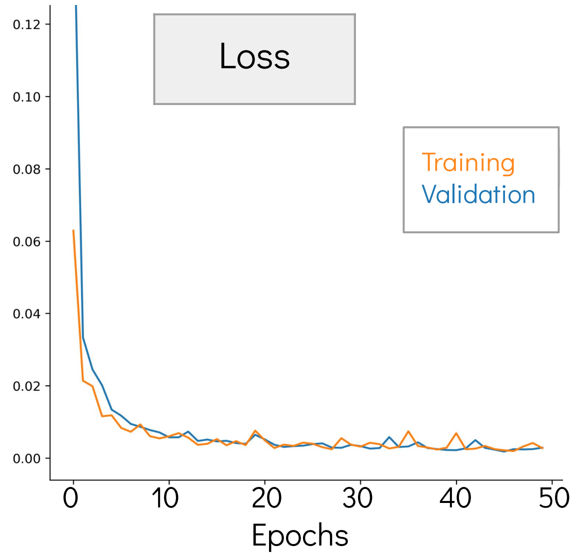
Results: Sample Performance

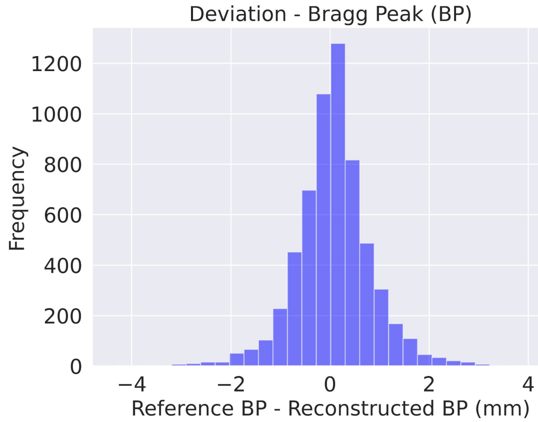
U-Net

TransBTS

SwinUNETR







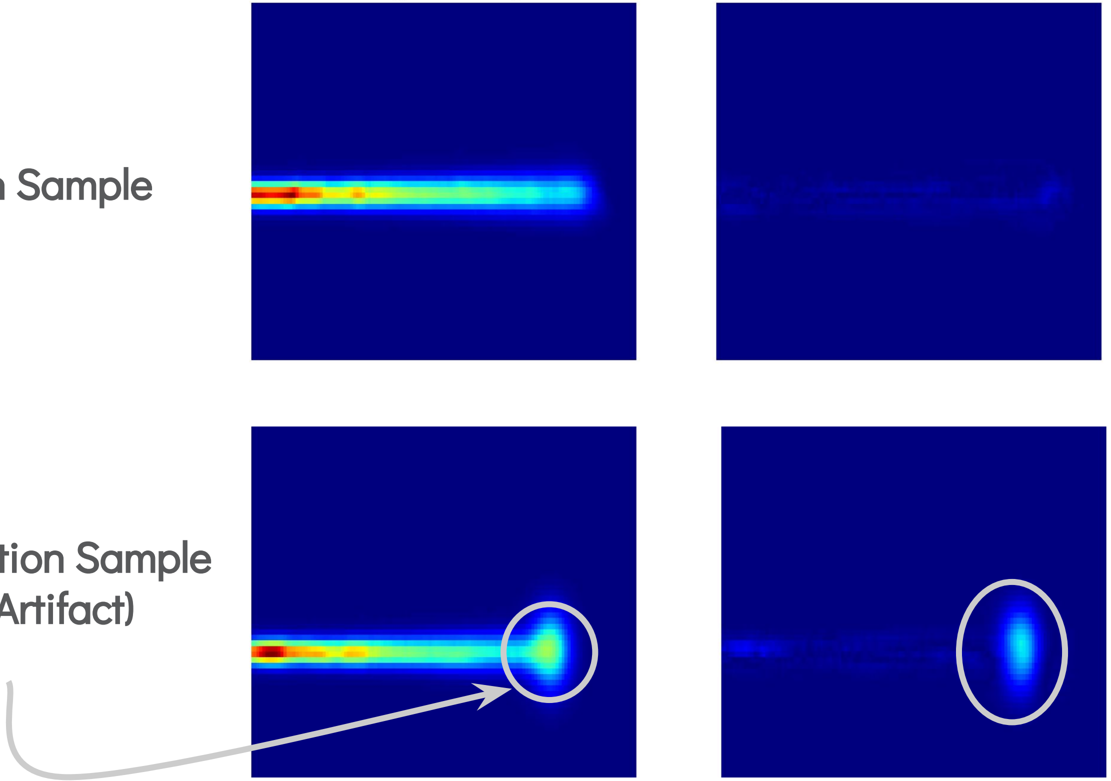
Results: Out-of-distribution Sample Detection

Activity (Input)

Final Error (3 iterations) |Estimated - Input|

In-Distribution Sample

Out-of-Distribution Sample (Gaussian Artifact)

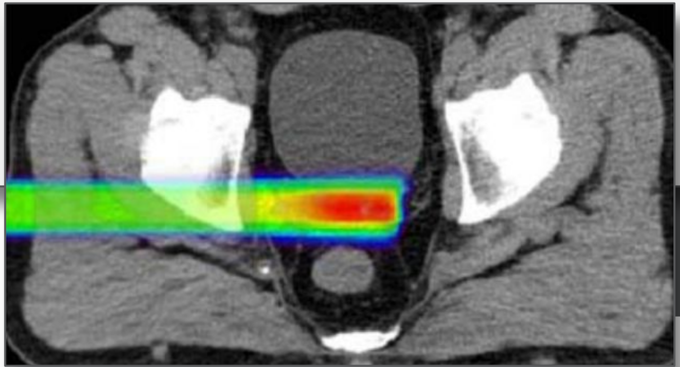


Discussion

- Robust, scalable models improved by training with gamma index
- Fast enough:
  4h Simulation + Training < 24h between CT and treatment.
- Sub-millimeter precision

Future Work

- Train with PET-reconstructed activity
- Include Spread Out Bragg Peaks (sum of many beams)
- Explore diffusion-based models
- Extend to Prompt-Gammas



Spread Out Bragg Peak

Onecha et al. 2021

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Thank you for your attention!

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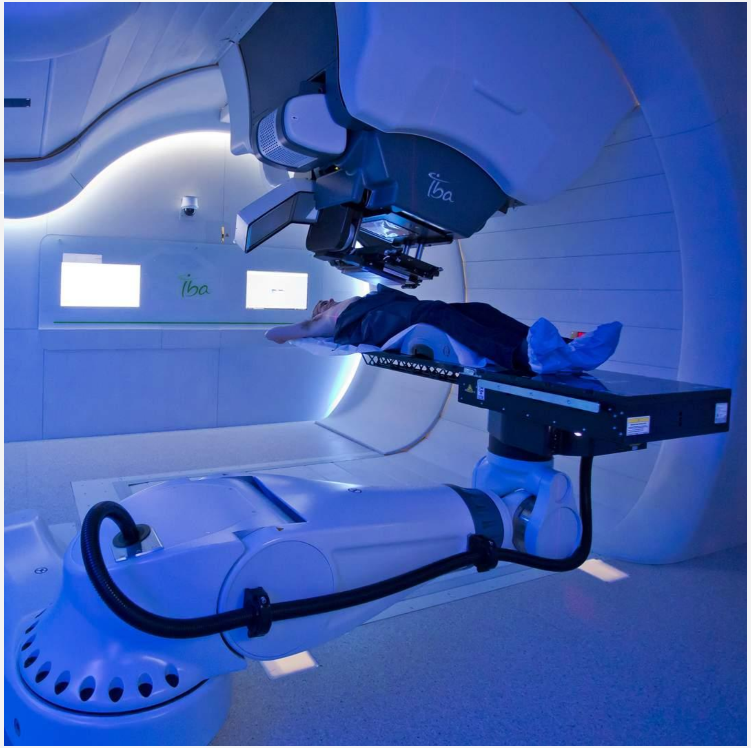

Quironsalud proton therapy facility, Madrid