



Do we need **clinical trials** in  
particle therapy and how can  
**medical physics** support  
them?

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# Agenda

- Introduction (Reinhard Schulte, Loma Linda University, UCSF)
- Clinical trials for protons and ions – needs, status, controversies (Hak Choy, UT Southwestern)
- Physics support and QA (Page Taylor, IROC, Houston)
- Computational phantoms to support clinical trials (Choonsik Lee, NCI)
- Plenary discussion (Audience & Speakers)

# Historical Perspective

- Photon therapy evolved from orthovoltage, to megavoltage (60Co, Linac) to 3D-conformal, to intensity-modulated, to image-guided, to adaptive radiation therapy
- Wait, why did not evolve to particle therapy recently, and will ions therapy the ultimate step?
- And if we know that it is technologically more advanced than anything we had before, more effective in many tumors (ions), and more sparing for normal tissues, why do we need clinical trials and clinical evidence before we use protons?

# The answer is not that simple!

- Most of the **technological developments** that lead to improved dose distributions with better normal tissue sparing, **evolved in the world of photon therapy**, and all **photons are governed by the same physics** (dose build-up followed by an exponential decay)
- Protons and ions delivery **fundamentally different dose distributions**, they also have a **depth-dependent RBE**, which depends on many delivery-and patient-specific factors and is often not well understood; they are **very sensitive to changes in tissue densities** during and between treatments requiring additional beam-specific distal and proximal margins; have a **different lateral scattering mechanism** than photons, leading to increase of penumbra with depth; lastly they **generate neutrons** in inelastic interactions
- Altogether, these factors may lead to **different side-effect profile for both early and late effects** that we need to investigate in well-designed **prospective clinical trials**

# But should all proton/ion patients be treated in randomized clinical trials?

- The answer is clearly “no”.
- Randomized trials are not needed when:
  - **sufficient evidence has been established** (proton therapy of base of skull tumors)
  - the dosimetric advantage is so obvious that **there is no equipoise** (pediatric tumors)
- In common tumors, where the intermediate-to-low dose sparing advantage is large and most likely important (breast, lung, liver), **randomized trials can be justified** (although the discussion is not over!)
- There has to be a “watch dog”, ensuring that procedures are done according to protocol (**trial QA**), but also to **find occasional patients** where the dosimetric difference warrants assignment to the proton trial
- These are **responsibilities of the medical physicist**

# The Role of the Medical Physicist

- Develop, learn, train others in procedures related to treatment planning, dosimetric evaluation, patient setup, in-room image guidance +/- treatment plan adaptation (if part of protocol)
- Provide support for other personnel involved in the trial (physicians, dosimetrist, therapists)
- Report on ongoing trials and results related to medical physics at national and international meetings (AAPM, WCMP, ASTRO, ESTRO, etc.)

# What are typical requirements for participation in a proton trial?

- 20% 1. Treat >100 patients with prostate cancer
- 20% 2. Complete an online training process
- 20% 3. Train staff and perform phantom tests
- 20% 4. Only perform a dosimetry check
- 20% 5. There are no specific requirements

Answer: 3– Train staff and perform phantom tests

[http://rpc.mdanderson.org/rpc/Services/Proton\\_Approval/Approval\\_process.htm](http://rpc.mdanderson.org/rpc/Services/Proton_Approval/Approval_process.htm)