Provocative Questions for Medical Physics in Oncology

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PQ for Med Phys (in Oncology)

- **Goal:** to define highest-level problems in oncology that medical physics should attack
- Two-day meeting on Oct 31/Nov 1 2016 in Boston
- Modelled after **NCI's Provocative Questions** (great input from Ed Harlow, Harvard University)
- Very diverse panel (see next page)
- Additional input from AAPM membership at large

Participants

- **Orly Alter**, University of Utah (Physics; Genomics Signal Processing)
- **Robert H. Austin**, Princeton University (Physics; Evolution)
- **Mike Carducci**, Johns Hopkins University (Medical Oncology; Prostate Cancer)
- **Mariam Eljanne**, NIH/NCI (Microbial Genetics; Physical Sciences in Oncology)
- **Sui Huang**, Inst for Systems Biology (Molecular/Cell Biology; Complex Systems)
- **Glenn Liu**, University of Wisconsin (Medical Oncology; Phase I)
- **Mike Makrigiorgos**, Dana Farber Cancer Institute (Physics; DNA technologies)
- **Larry Marks**, University of North Carolina (Radiation Oncology; Lung Cancer)
- **Lance Munn**, Harvard University (Chemical Engineering; Angiogenesis)
- **Thea Tlsty**, University of California San Francisco (Pathology; Malignancy)
- **George Wilding**, MD Anderson (Medical Oncology; GU Oncology)
- **Rock Mackie**, University of Wisconsin (Medical Physics)
- **Jeff Siewerdsen**, Johns Hopkins University (Medical Physics)
- **Thomas Bortfeld**, Massachusetts General Hospital (Medical Physics)
- **Robert Jeraj**, University of Wisconsin (Medical Physics)

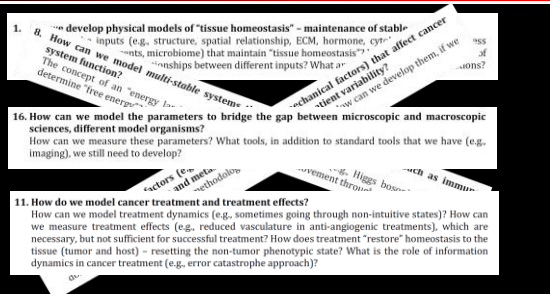
Provocative Questions Workshop

1. What are the **top 3 unanswered questions** in cancer – from your viewpoint (be provocative)? - for MDs only: What are the top 3 unanswered questions in your clinical practice?
2. What is the **unique physics angle** from which physical scientists can approach these questions?
3. What are the **barriers** that we face in trying to answer the questions?

Provocative Questions

- Started with **150+ questions** (about half from AAPM members)
- Reduced them to **18 Provocative Questions**
- Identified **10 Barriers** (see next talk)
- **Medical Physics "Translation"** remains the main challenge

Examples of Provocative Questions



Provocative Question Translation

- **Pilot** between University of Wisconsin and MGH
- Selected a **PQ paper** (metastases), and started **translation** to medical physics

Article overview

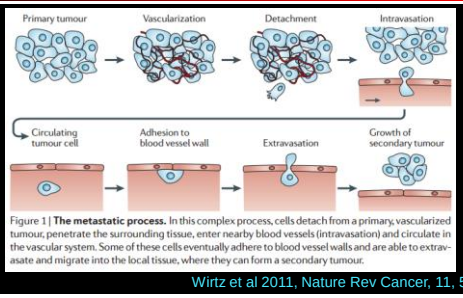
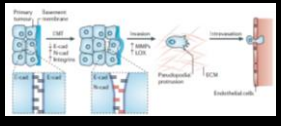


Figure 1 | **The metastatic process.** In this complex process, cells detach from a primary, vascularized tumour, penetrate the surrounding tissue, enter nearby blood vessels (intravasation) and circulate in the vascular system. Some of these cells eventually adhere to blood vessel walls and are able to extravasate and migrate into the local tissue, where they can form a secondary tumour.

Wirtz et al 2011, Nature Rev Cancer, 11, 512-522

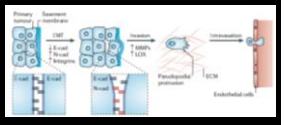
Physical interactions in invasion

- **Epithelial–Mesenchymal Transition (EMT)** is initial step in invasion
  - Detachment of carcinoma cells from basement membrane (and primary tumor)
  - Tumor cells digest basement membrane
  - Tumor cells traverse ECM in search of blood vessel
    - Mechanical properties (stiffness) of ECM can drive invasion
    - Collagen likely plays a role
- **In vitro studies** to investigate invasion
  - Cell mobility not always the same and 3D cultures
- **Intravital microscopy** technique to vitro studies and study invasion tissues



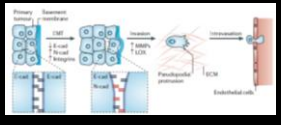
Physical interactions in invasion

- **Physics concepts**
  - Can imaging play a larger role in studying tumor cell invasion and related EMT?
  - …



Physical interactions in invasion

- **Physics concepts**
  - Can imaging play a larger role in studying tumor cell invasion and related EMT?
- **Discussion**
  - What fraction of tumor cells are actively invading nearby vasculature vs. passively ‘falling into’ tumor vasculature?



PQs: Characters and Forces

- **What are the physical (in addition to biological) factors that drive the different mechanisms of cell migration?** [PQ 6]
  - What are the factors of the cell, and what the factors of the environment driving this?
  - Which of the factors are the most important, most targetable, most measurable?
  - What are the distinct differences between migrating and non-migrating cells?
- **What are the characteristics of metastasizing vs. non-metastasizing cells?** [PQ 2,7]

Future plans

- Increase **Provocative Questions Awareness**
  - Let us know if you are interested !
- Continue **Provocative Questions Translation**
  - Let us know if you are interested !
- Explore **Provocative Questions Funding Opportunity**
  - Let us know if you are interested !
- **International efforts**
  - Europe (ESTRO future workshop in 2018)
  - Australia (EPSM future workshop in 2018)