## Immunotherapy Killed the IGRT Star

#### https://www.youtube.com/watch?v=lwuy4h HO3YQ&feature=youtu.be



#### Learning objectives

- Learn about the role of radiation as an immune booster in cancer therapy
- Summarize ongoing clinical trials combining radiation and immunotherapy
- 3) Discuss the evolving role of IGRT



### A Physicist's Cliff Notes to Immunotherapy

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#### Disclosures

- I receive royalties from the University of Chicago for software licensed for computer aided detection of breast cancer.
- ▶ I am co-Chair of TG-302: Surface Image Guided RT.
- I serve as Physics PI on NRG/Alliance/institutional clinical trials.



#### Outline

- 1. Overview of immunotherapy definitions/principles
- 2. Review of the role of IGRT for accurate targeting of tumors in SBRT
- 3. Discuss role of IGRT with shifting goal of radiotherapy is to induce an immune response



# **1. Overview of Immunotherapy** Definitions/Principles



#### Definitions

- Immunotherapy harnesses the body's immune system to fight cancer
- Types of immunotherapy:
  - Monoclonal antibodies flag cancer cells, block immune system inhibitors (e.g., Pembrolizumab)
  - Oncolytic virus therapy genetically modified virus to kill cancer cells
  - T-cell therapy genetically modify T-cells to kill cancer
  - Cancer vaccines triggers immune system by exposing it to an antigen

www. Mayoclinic.org www.Cancer.net.

#### Principles

 Radiation can induce an immune response (Weichselbaum et al., "Radiotherapy and immunotherapy: a beneficial liaison?")





#### Principles

- Radiation can induce an immune response<sup>1</sup>
  - Is there a dose threshold? <sup>2</sup>
  - Is there tumor volume threshold? <sup>2</sup>
  - Can this immune response treat tumor cells that are not directly irradiated (i.e., abscopal effect)? <sup>3</sup>
  - 1) Weichselbaum et al., "Radiotherapy and immunotherapy: a beneficial liaison?"
  - 2) Chajon et al, "The synergistic effect of radiotherapy and immunotherapy: A promising but not simple partnership."
  - *3) Jatoi, et al, Hypothesis: can the abscopal effect explain the impact of adjuvant radiotherapy on breast cancer mortality?*



#### 2. Role of IGRT in SBRT

#### Tumor Targeting



#### IGRT

- Imaging in the treatment room<sup>1</sup>
  - Reduces geometric uncertainty
  - Improves agreement between planned and delivered dose





#### **IGRT for SBRT**

- IGRT has enabled SBRT & other hypo-fractionated RT
- Does the role of IGRT differ if treatment intent is immuno-modulation instead of total ablation?





Luke et al., "Safety and Clinical Activity of Pembrolizumab and Multisite Stereotactic Body Radiotherapy in Patients With Advanced Solid Tumors"

#### **IGRT for SBRT**

- Is localization accuracy as important for immunomodulation as for ablation?
- Did video kill the radio star?
- Did immuno kill the IGRT star?



#### **Discussion points**

- What clinical evidence exists that radiation is an immune modulator before the introduction of immunotherapy?
- 2. How will the optimal timing and dose of radiation in relationship to immunotherapy be determined?
- 3. What is the role of IGRT if the intention is no longer to deliver dose to the entire tumor volume?



# Thank you for your attention!



