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Disclosures

I have nothing to disclose.
Cancer is a dynamic system!

In vitro cellular growth

\[ y = c e^{0.4938x} \]

Days since plating

In vivo multicellular spheroid growth

\[ \frac{dV}{dt} = T_{pot} V (1 - \frac{V}{V_{sat}}) \]

Growth slows down

Late growth approaches zero

Proliferation saturation
Proliferation saturation in cancer

Individual patients present in the clinic with an individual Proliferation Saturation Index (PSI). PSI may then serve as a prognostic marker for patient-specific radiation therapy responses.

$\frac{dV}{dt} = AV \left(1 - \frac{V}{V_{sat}}\right) - pSV \left(1 - \frac{V}{V_{sat}}\right)$

intrinsic tumor growth rate
intrinsic RT response rate
Dirac delta for RT fractions

PSI in Non-small cell lung cancer

Sunassee et al., Int. J. Radiat. Biol., 2019
Can we predict the response to fractionated radiation before treatment on a per patient basis?

How to change treatment for patients predicted to fail?
PSI determines volume regression

- "Standard of care"
- "Hyper-fractionation"
- "Hypo-fractionation"

\[
\text{PSI} = 0.99 \quad \text{PSI} = 0.66 \quad \text{PSI} = 0.33
\]

Latifi et al, ASTRO 2017
Prospective PSI calculation

\[ \text{PSI} = \frac{V_{\text{T1} \text{TX}}}{V_{\text{DIAG}} \times (e^{\text{M1}} - 1)} \]

NCT03656133

Phase II Protocol to Test Proliferation Saturation Index to Personalize Radiation Therapy Fractionation for Patients with Squamous Cancer of the Head and Neck

- Simple mathematical model
- one variable, one term, one parameter
- to learn patient-specific growth dynamics
- to predict response to radiotherapy
- to personalize fraction to maximize response
- evaluate response in N=1 trials

62 patients
Response Evaluation Criteria In Solid Tumors (RECIST)

- **Complete Response (CR)**: Disappearance of all target lesions.
- **Partial Response (PR)**: At least a 30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD.
- **Stable Disease (SD)**: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started.
- **Progressive Disease (PD)**: At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

- GTV
  - Sim 5 wks
  - Dx
  - +41%: Progressive Disease
  - Response !!!
  - No Response !!!

- Adaptive control with a reference model

  - Enderling et al., Trends in Cancer, 2019
Quantitative approaches will not replace the oncologist!
The oncologist who uses quantitative approaches may replace the oncologist who does not.

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