Treatment of oligo-resistant and oligo-progressive disease in metastatic prostate cancer patients with radiation therapy

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INTRODUCTION

- The eventual development of acquired resistance to systemic therapy is inevitable in metastatic prostate cancer patients (mPC)
- Even at the time of progression, most of a patient's disease may still be responding to the current treatment [1]
- Patients with only 5% of lesions progressing may have shorter progression-free survival [2]
- **The purpose of this work is to propose a workflow to supplement systemic therapy that is effectively controlling most of the disease with a local radiation therapy (RT) to non-responding disease in mPC patients (Figure 1)**

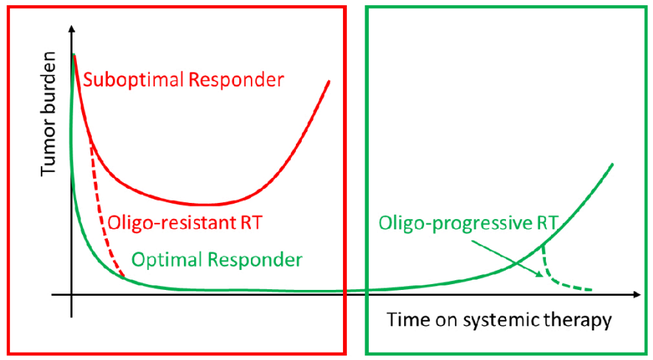


Figure 1: Schematic of potential patient response types. Patients who experience limited benefit from systemic therapy are suboptimal responders. We propose that suboptimal responders with limited resistant disease (**oligo-resistance**) be treated with RT to "rescue" their response to that of the optimal responder (red dashed line).

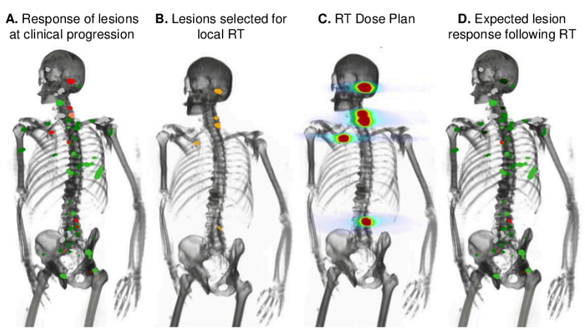
Optimal responders would be treated with RT to **oligo-progressive** disease to prolong benefit to the systemic therapy (green dashed line).

METHODS

- 21 bone-mPC patients treated with systemic therapy (enzalutamide)
- ^{18}F-NaF PET/CT scans at baseline, after 12 weeks, and at progression or year 2
- Lesions response was classified into completely responding (iCR), partially responding (iPR), stable disease (iSD), progressive disease (iPD), new disease (iND) based on the relative change in total lesion burden (iSUV$_{total}$) [3]

Proposed workflow:

A. Lesion response is categorized at the time of week 12 and clinical progression
B. Five fields covering iPD+iND lesions are selected to receive RT
C. RT dose plan generated for the five selected fields
D. Expected response of patient is calculated following RT, assuming complete response of the five targeted fields



In **A** and **B**, the CT maximum intensity projection (MIP) is overlaid with lesions colored by their response category. In **C**, the skeleton is shown for reference; treatment planning was performed on the full CT scan of the patient's PET/CT and future clinical trials will plan based on a standard simulation CT.

RESULTS

Radiation therapy to treat oligo-resistant disease

- Patients had a median of 10.2% (0.0-94.7%) iPD+iND lesions at week 12
- 11/21 patients were suboptimal responders and were evaluated for oligo-resistant disease
  - The median percentage of SUV$_{total}$ targeted by the five RT fields was 8.4% (range 0.0-85.7%)
  - 6/11 suboptimal responders had oligo-resistant disease and were eligible for RT (expected ΔSUV$_{total}$≤-25%)

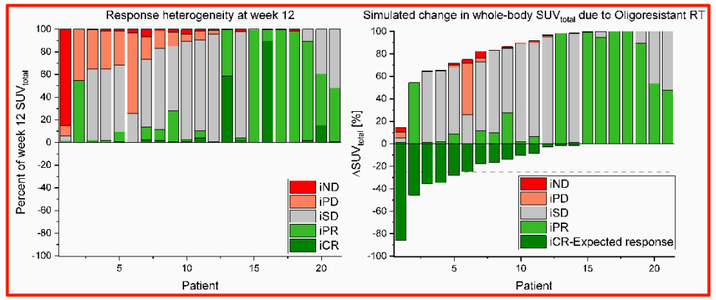


Figure 3: Evaluation of oligo-resistant RT. Left: Percent of disease burden (SUV$_{total}$) in each response category at week 12. **Right:** Six out of 21 patients were eligible for oligo-resistant RT as the elimination of the 5 selected RT fields would result in ΔSUV$_{total}$≤-25%. The impact of simulated RT was complete response. The impact of simulated RT was complete response [4].

Radiation therapy to treat Oligo-progressive disease

- Patients had a median of 5.3% (0.0-98.1%) of iPD+iND lesions at progression or year 2
- The median percentage of SUV$_{total}$ targeted by the five RT fields was 4.5% (range 0.0-90.8%)
- 2/8 patients had oligo-progressive disease and were eligible for RT (expected ΔSUV$_{total}$≤-25%)

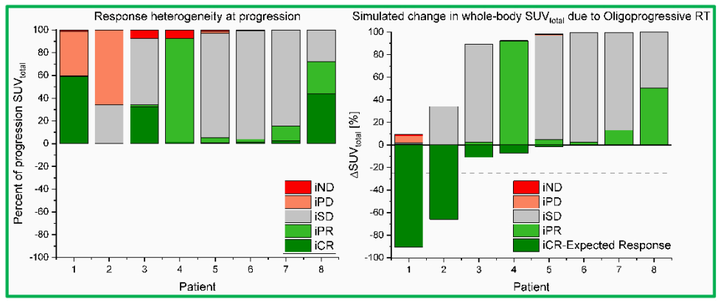


Figure 4: Evaluation of oligo-progressive RT. Left: Percent of disease burden (SUV$_{total}$) in each response category at progression or year 2. **Right:** Two out of 8 patients were eligible for oligo-progressive RT as the elimination of the 5 selected fields would result in ΔSUV$_{total}$≤-25%. The impact of simulated RT was complete response [4].

CONCLUSIONS

- This work proposed a new approach to selecting eligible mPC patients for oligo-resistant and oligo-progressive RT based on quantitative NaF PET/CT response
- The results suggest that roughly a third of bone-mPC patients treated with enzalutamide may benefit from added oligo-resistant RT and one quarter of patients from oligo-progressive RT
- Confirmation of survival benefits should be confirmed in a large randomized controlled clinical trial

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