Cyclic Changes of Absorbed Dose as a Biomarker for Radiological Response in Neuroendocrine Tumours Treated with [^{177}Lu]Lu-DOTATATE

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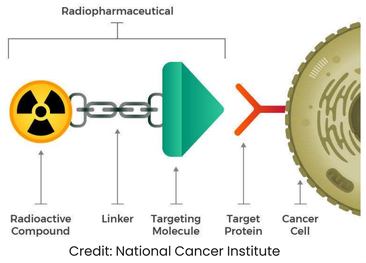
INTRODUCTION

Current [^{177}Lu]Lu-DOTATATE treatment protocols for neuroendocrine tumours (NET) apply fixed administered activities (AA) without individual optimization or absorbed dose (AD) calculations. Given the late-responding nature of NETs, identifying biomarkers that predict treatment efficacy could enable adaptive therapeutic strategies.



Credit: National Cancer Institute

METHODOLOGY

Patients with positive [^{68}Ga]Ga-DOTATATE scans and confirmed NETs were enrolled in the OZMOSIS OZM-067 trial (NCT02743741) and were treated with 4 cycles of [^{177}Lu]Lu-DOTATATE and imaged at 4, 24, and 72 hr post-injection after each cycle. The AA varied depending on kidney dose. Data from a subset of 73 patients is presented here who had tumours eligible for dosimetry. Response was defined as partial response (PR) as per RECIST guidelines, as opposed to stable disease (SD)

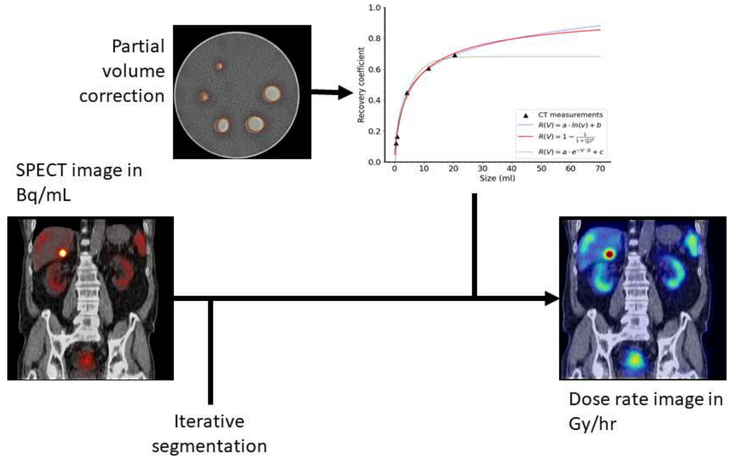


Figure 1. Tumours were segmented using an iterative thresholding technique that was expected to be reliable for volumes at least 10 mL in size. Recovery coefficient-based partial volume correction was applied to segmented volumes. The AD was calculated using a biexponential clearance model. If a patient had more than one eligible tumour, the average AD was recorded.

AD/AA DECREASES BETWEEN CYCLES

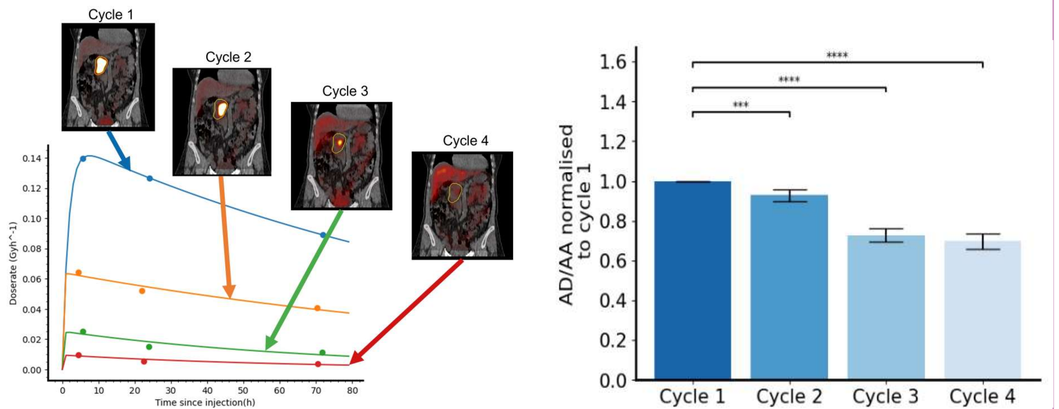


Figure 2. AD/AA is significantly decreased for later cycles when compared to the AD/AA of cycle 1. An example of a responding patient is shown on the left, and data for the whole cohort on the right. The average total change in AD/AA between cycles 1 and 4 (ΔAD/AA) was around -30%.

AD AND ΔAD/AA CORRELATE TO RESPONSE

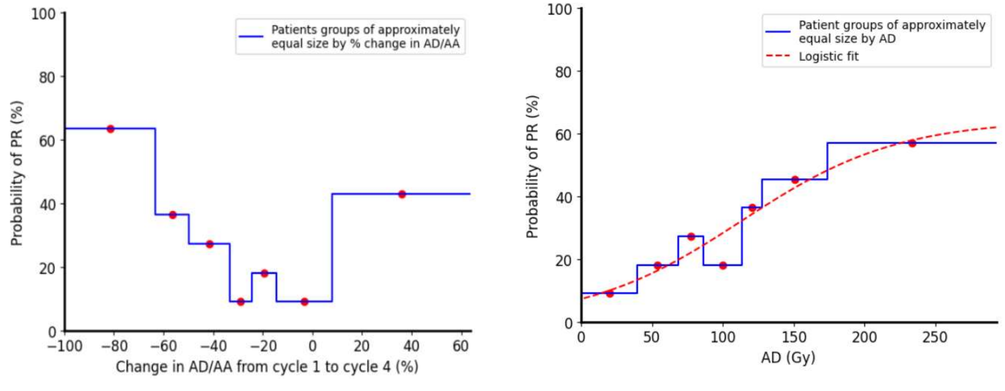


Figure 3. Probability of PR within patient subgroups defined by ΔAD/AA (left) or AD (right). Representative coordinates for each group are shown as red dots, which served also as the input into a logistic model fitting routine. Both imaging biomarkers are systematically related to PR. Note that the average AD for patients with positive ΔAD/AA was relatively high (>100 Gy).

AD AND ΔAD/AA ARE INDEPENDENT BIOMARKERS

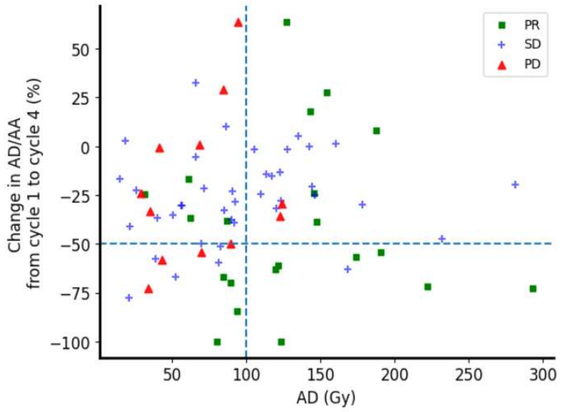


Figure 4. There is no obvious relationship between changes in AD/AA and AD. Response is unpredictable at low AD, and AD alone does not obviously predict PR. However, a combination of high AD and large changes in AD/AA seems to better stratify patients who eventually have PR. Dashed lines represent arbitrary cut-offs of 100 Gy AD and -50% change in AD/AA.

CONCLUSIONS

- AD/AA decreased significantly across cycles.
- Patients with PR presented with larger decreases in AD/AA and higher AD.
- AD and AD/AA could be used simultaneously as early imaging biomarkers of response

CONTACT INFORMATION

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