A Teaching Affiliate
of Harvard Medical School

Inferring the differential immunological impact of proton vs photon radiotherapy with TCR sequencing

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MASSACHUSETTS
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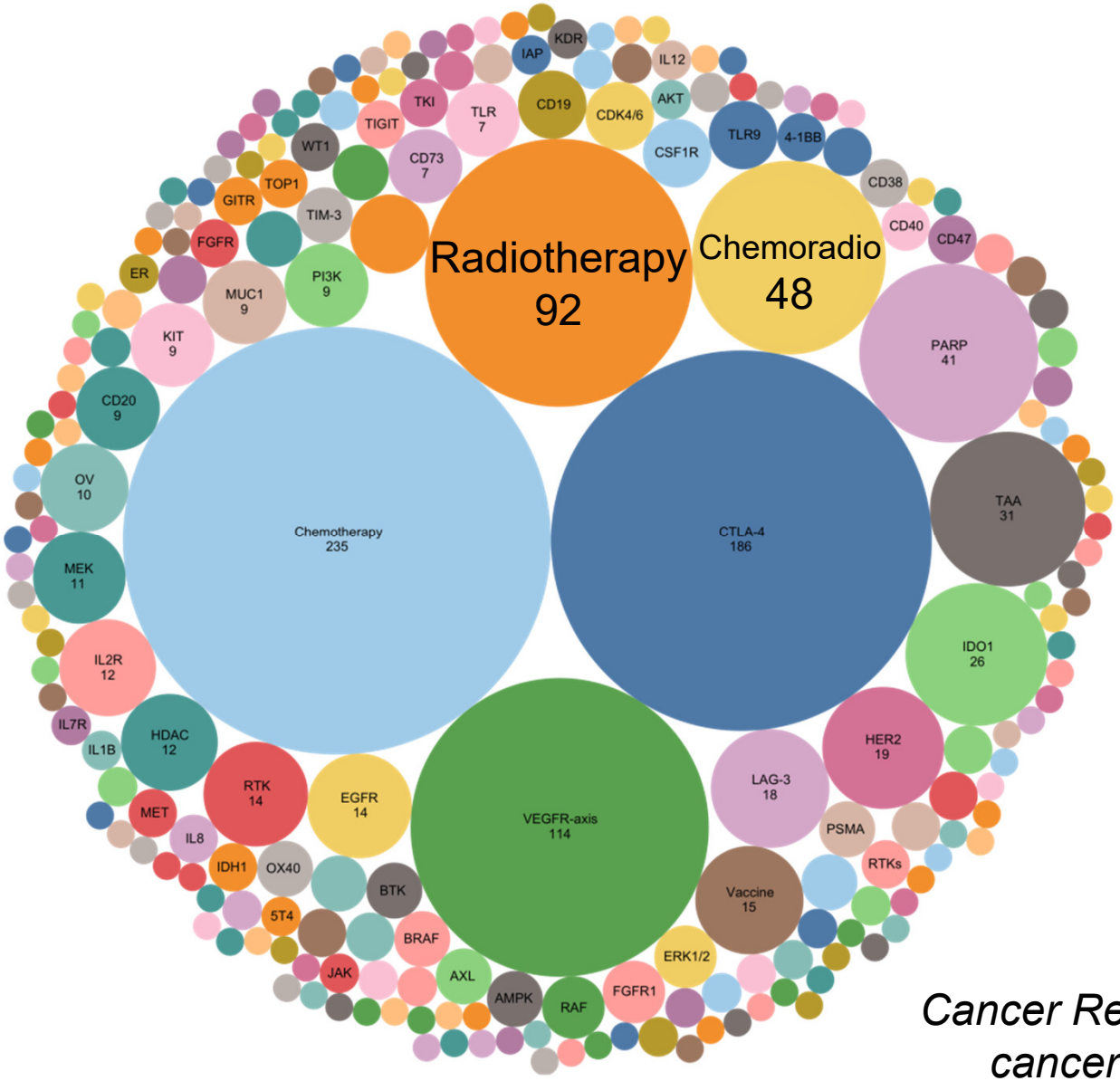
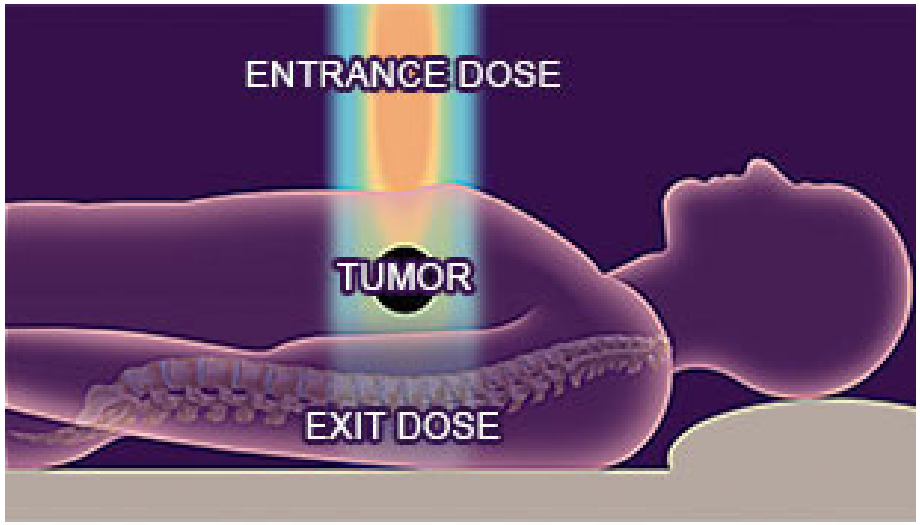
1,287 PD1/PD-L1 combination trials started in last 2 years



Cancer Research Institute, cancerresearch.org

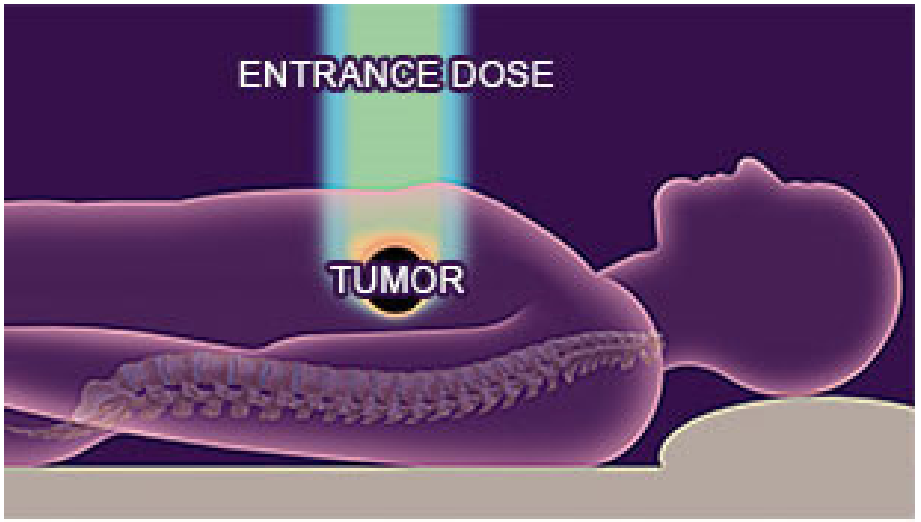
Photon vs proton based radiation therapy (RT)

Conventional photon-based RT



Most energy deposited
before target, some after

Proton-based RT

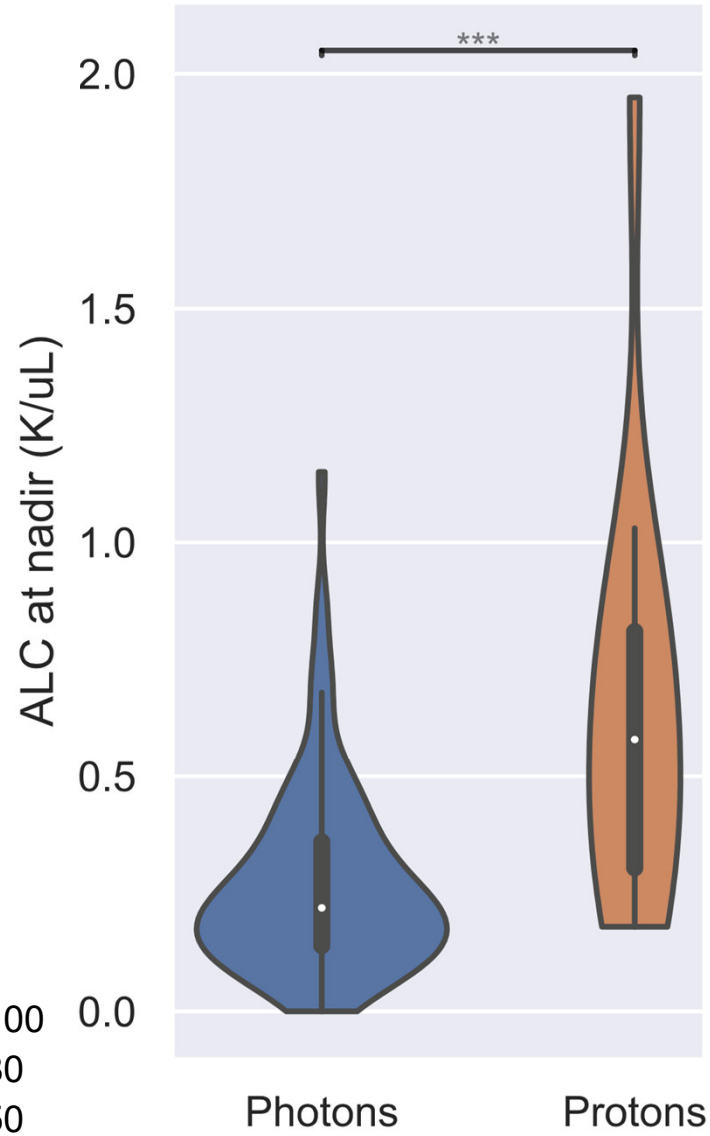


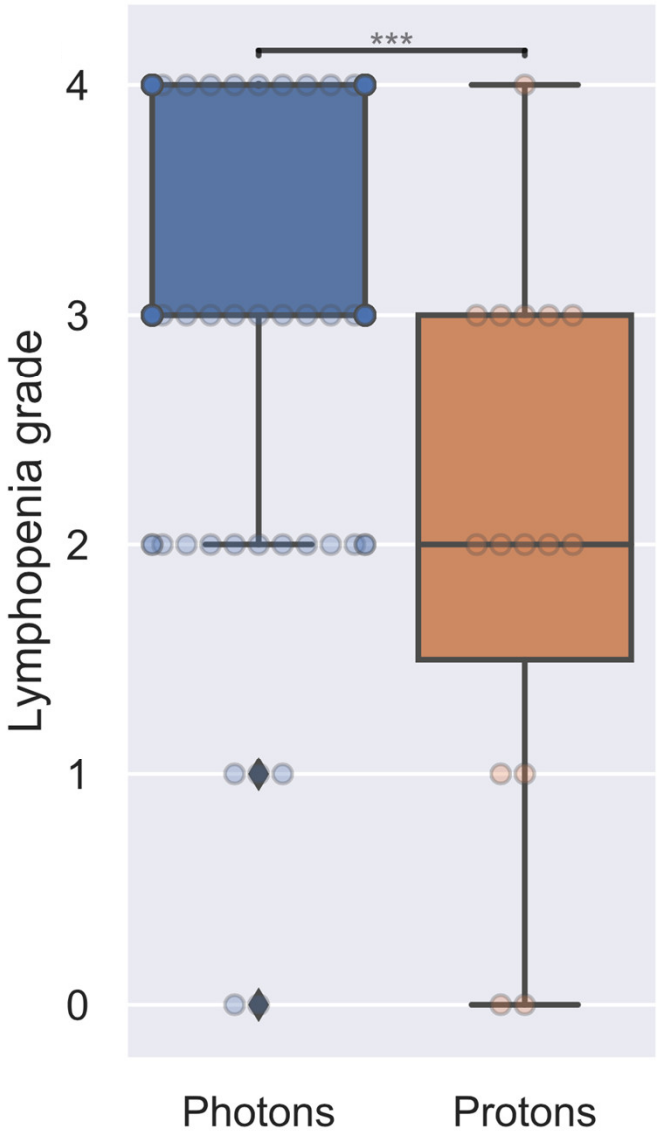
Most energy deposited
on target

>99% of patients
who receive RT

Hitchcock et al. (2017),
World J Gastrointest Surg

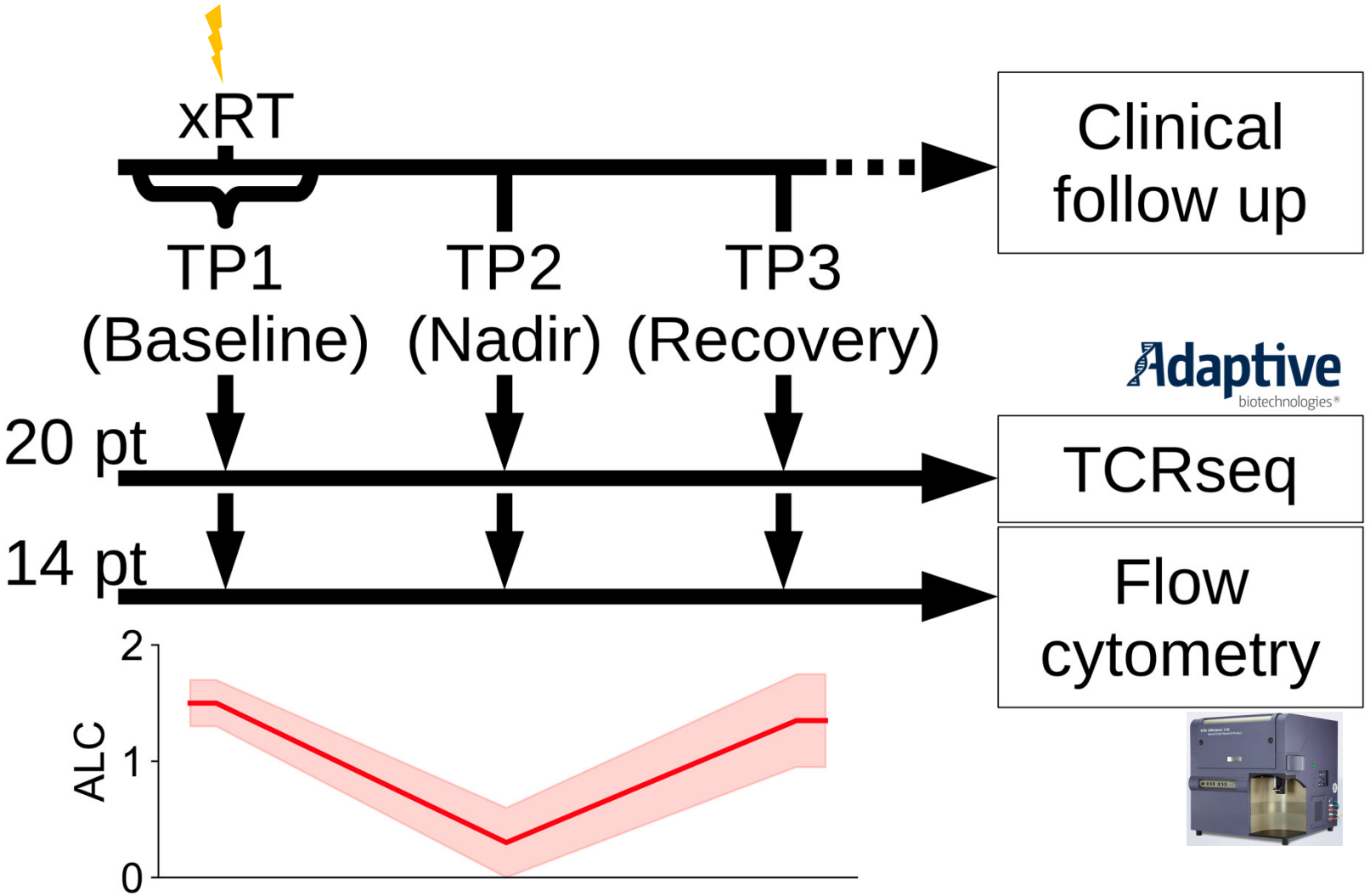
Radiation-induced lymphopenia



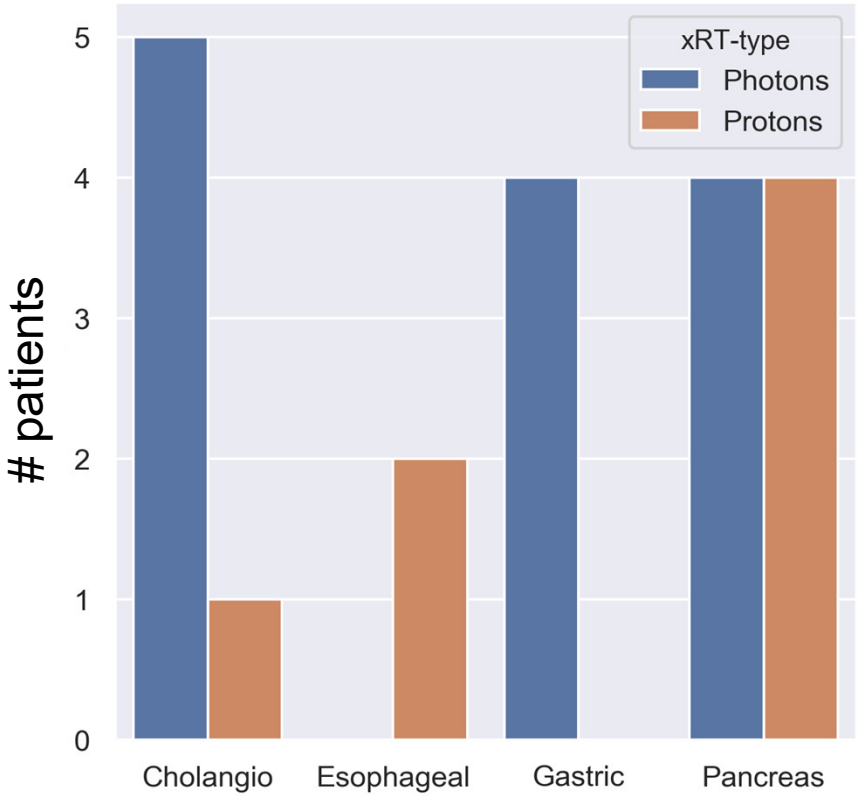


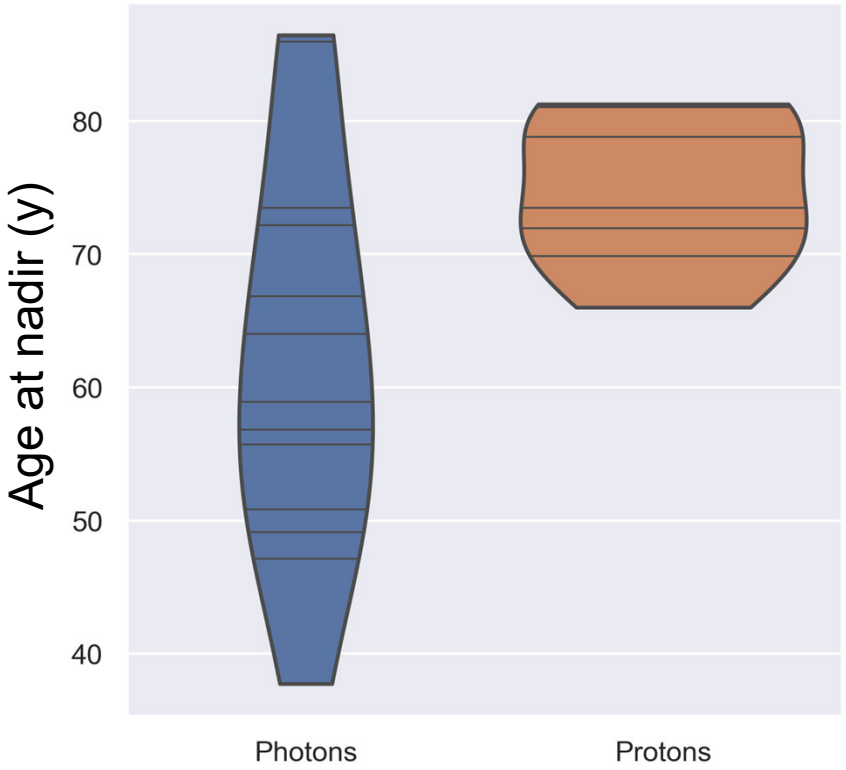
Grade:
1) 80 <= ALC < 100
2) 50 <= ALC < 80
3) 20 <= ALC < 50
4) ALC < 20

Patient sampling



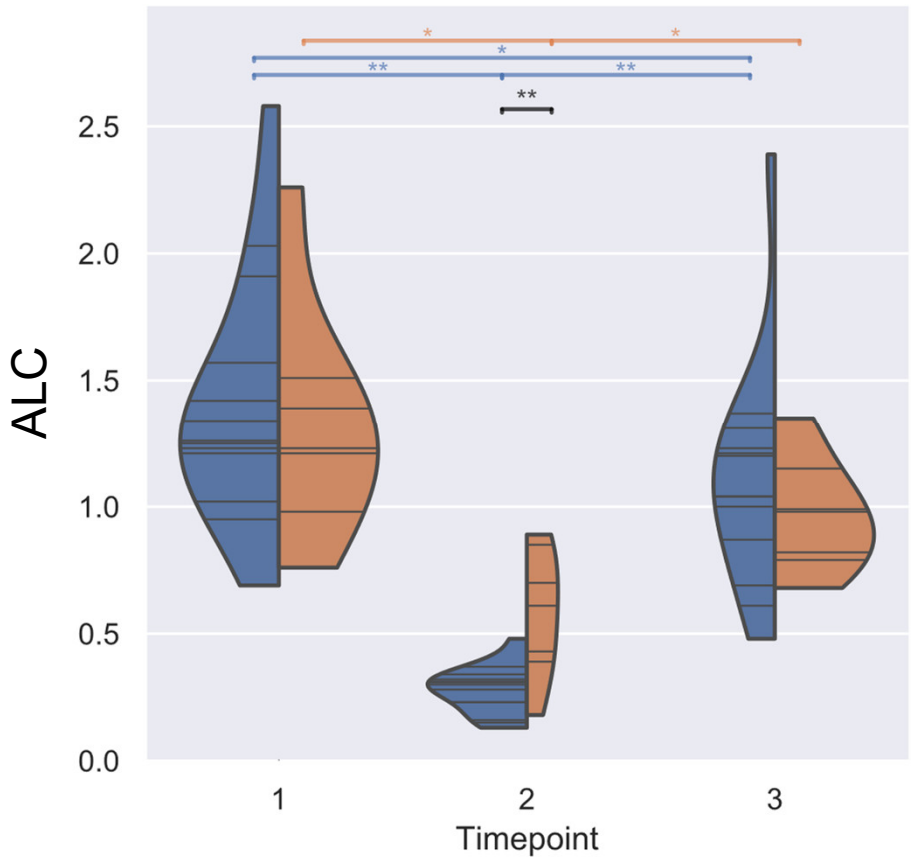
Patient/treatment overview

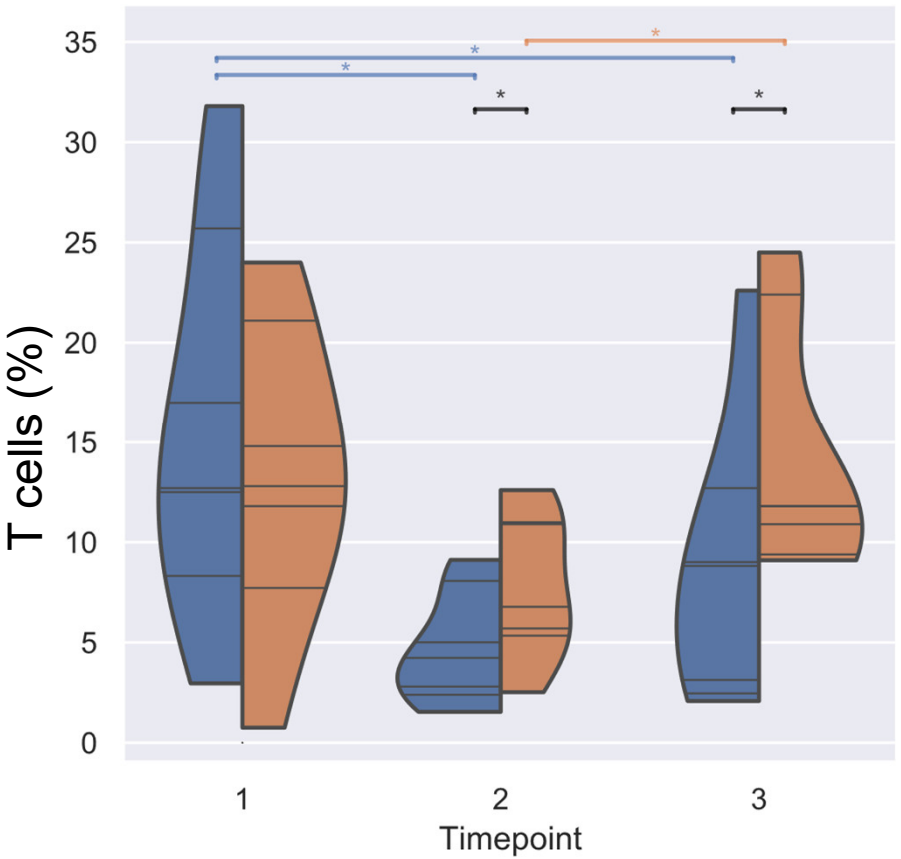




Radiation induced lymphopenia

ALC = absolute lymphocyte count

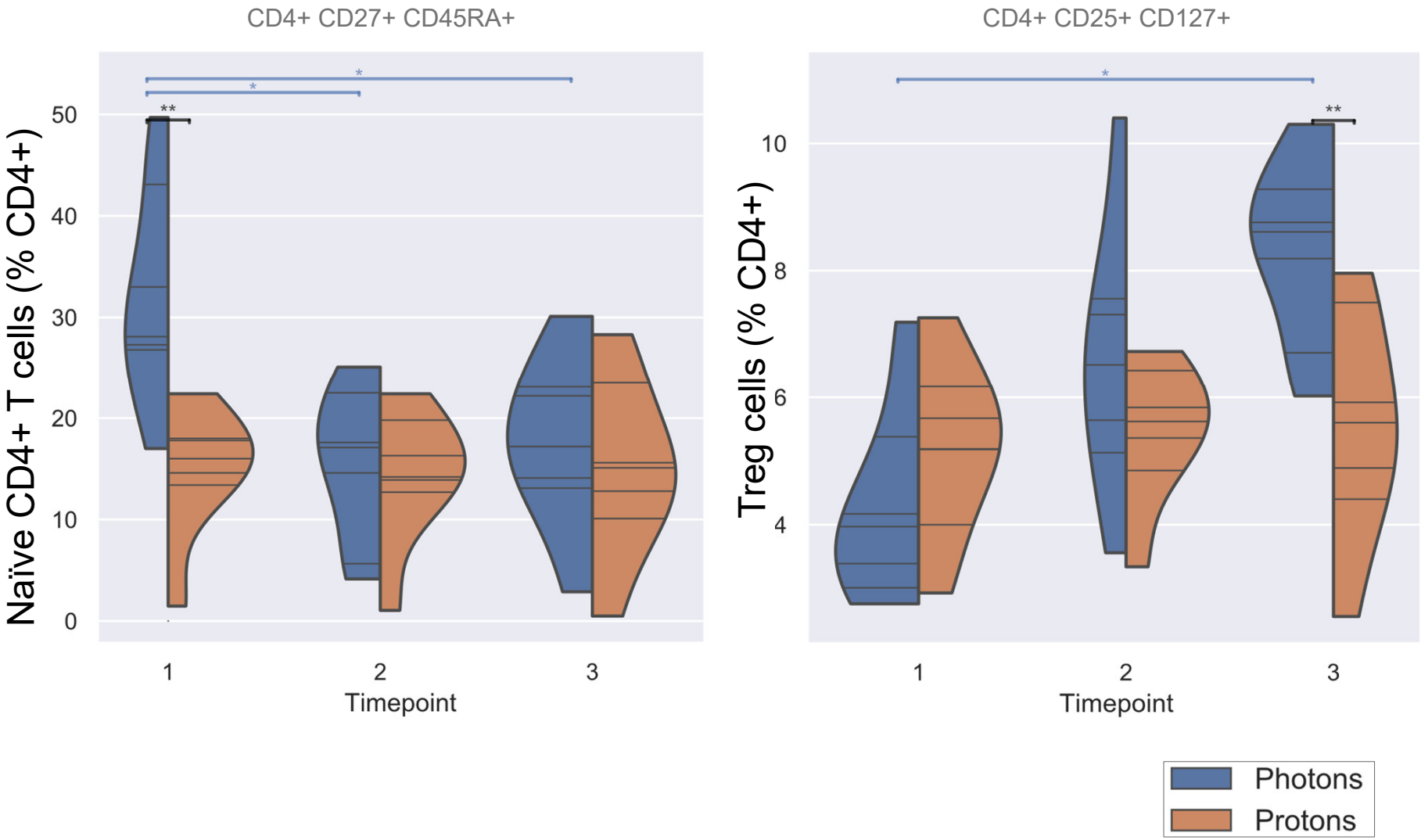




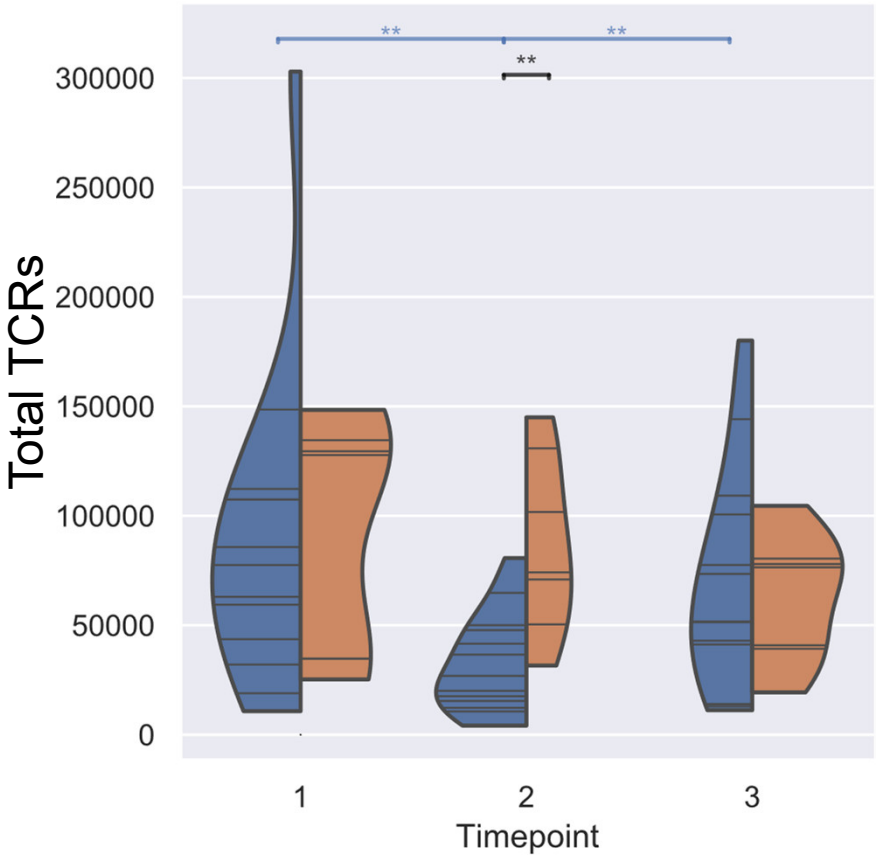
Photons
Protons

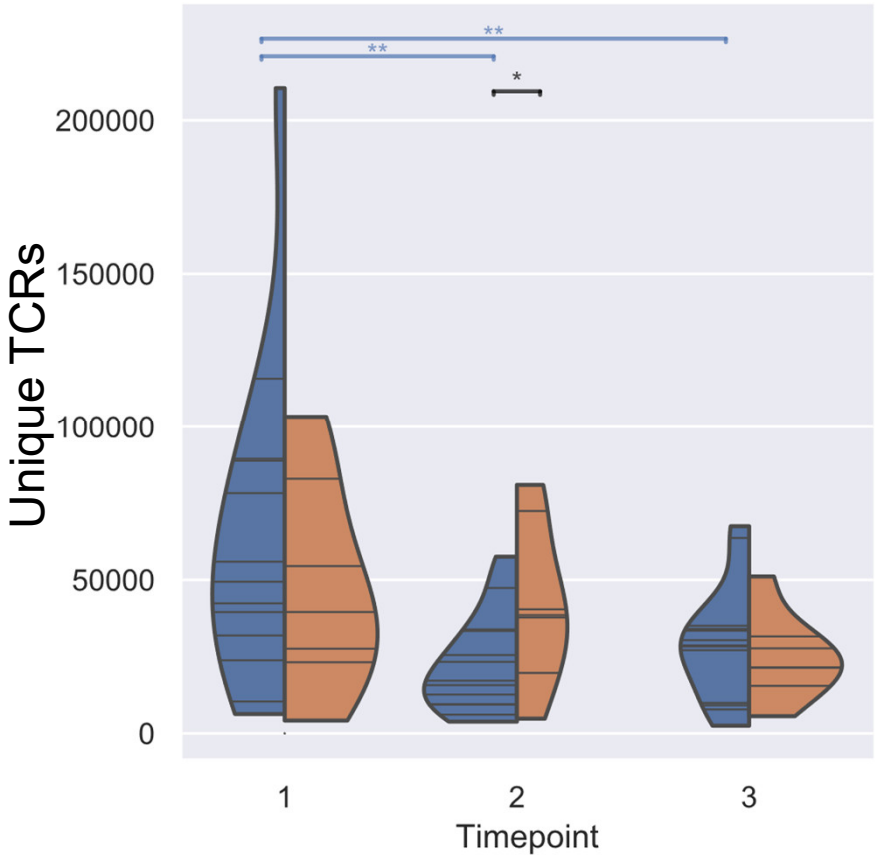
* = inter-group Mann Whitney U
/ = photon/proton intra-group Wilcoxon ranked sum

Photon-treated patients lose a lot of their naïve CD4+ T cells, and acquire more Tregs



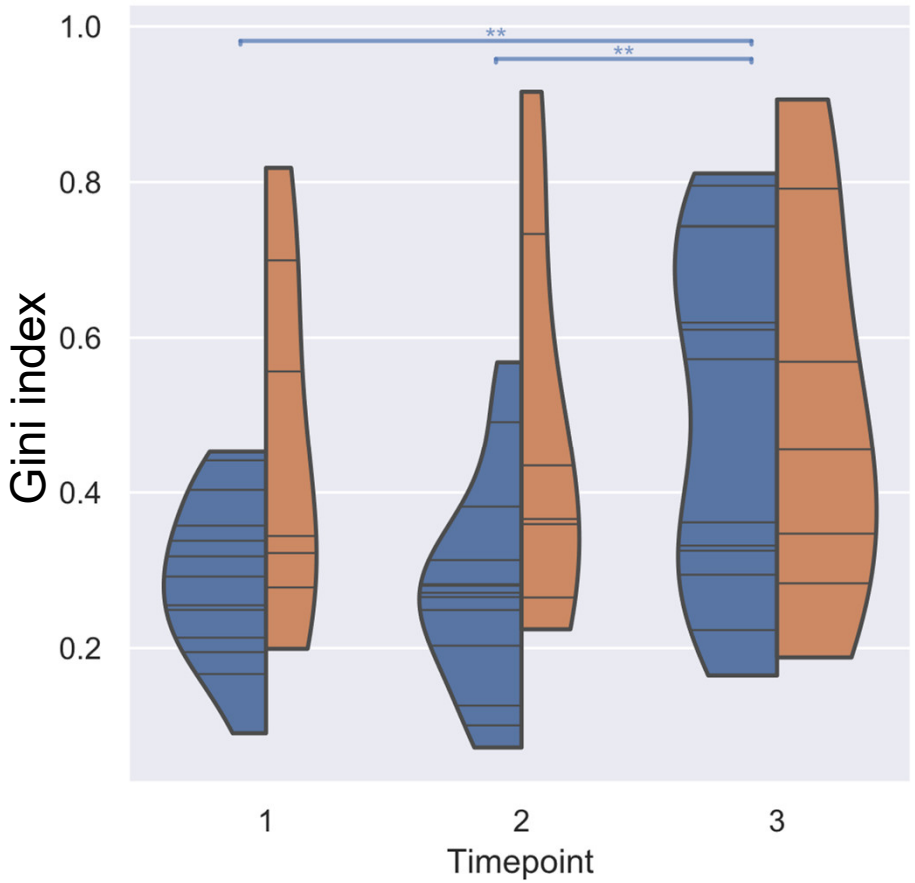
Photon treated patients total TCRb numbers contract & rebound, but unique numbers stay low post-nadir…

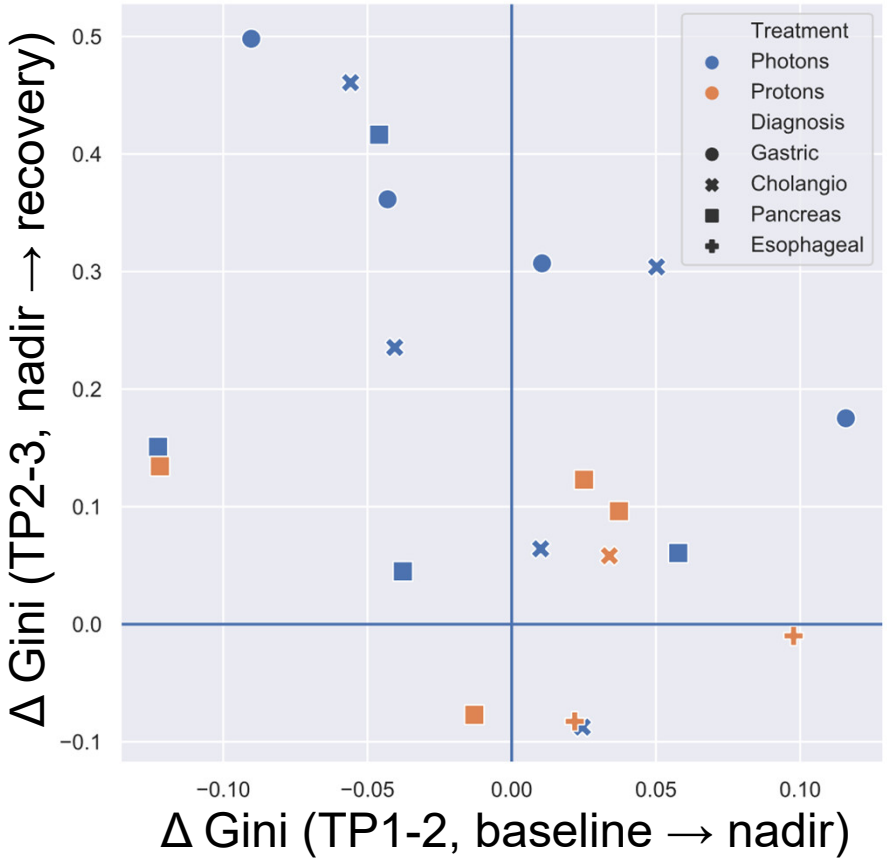




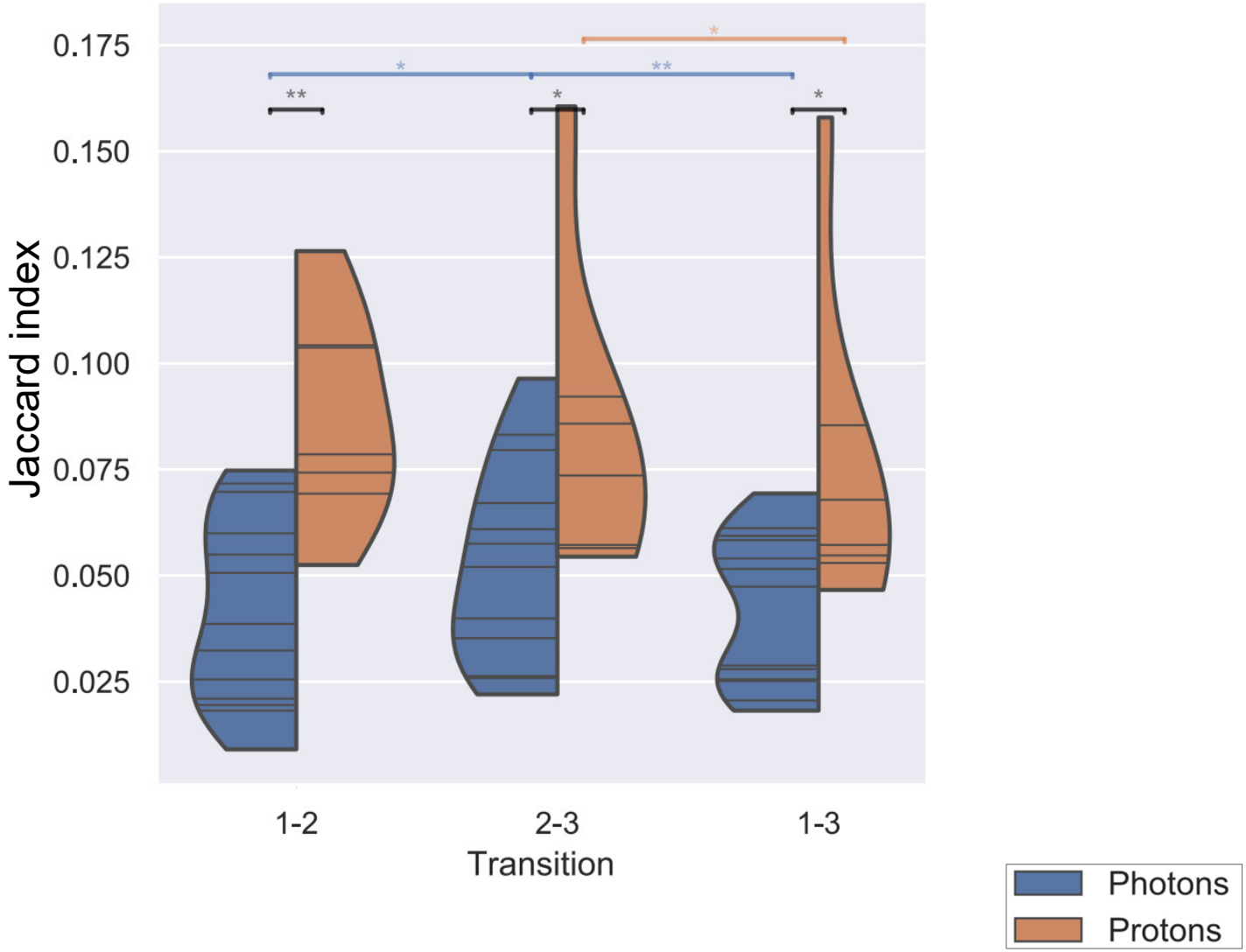
Photons
Protons

…corresponding to an increase in inequality

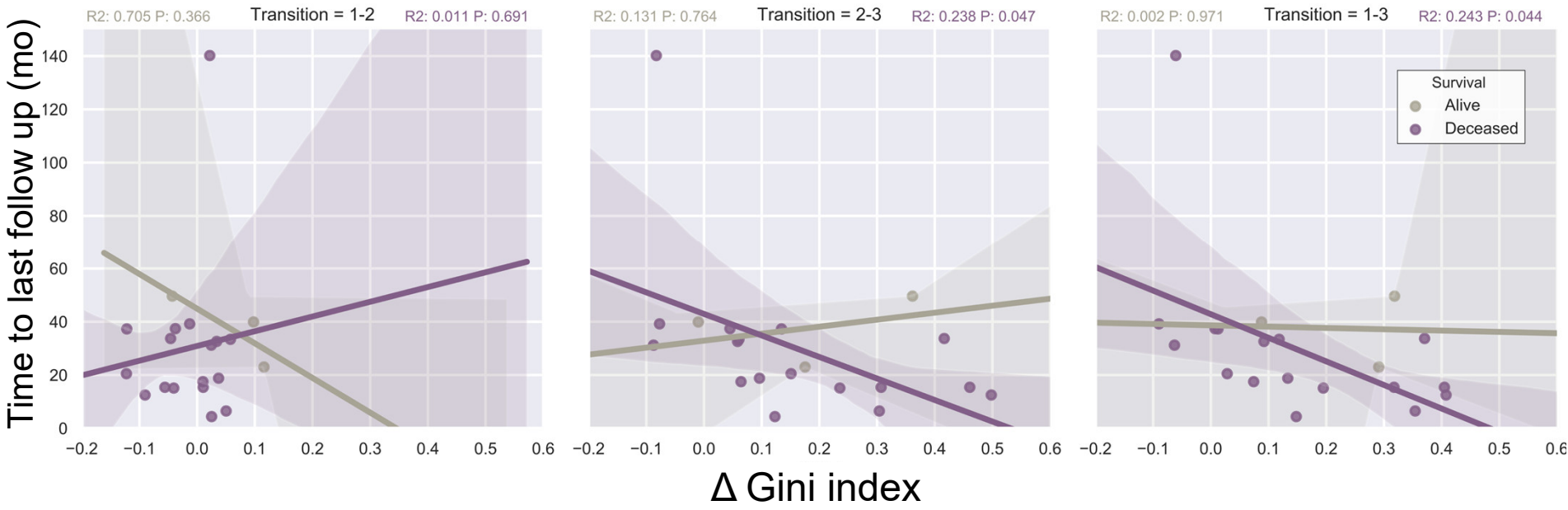




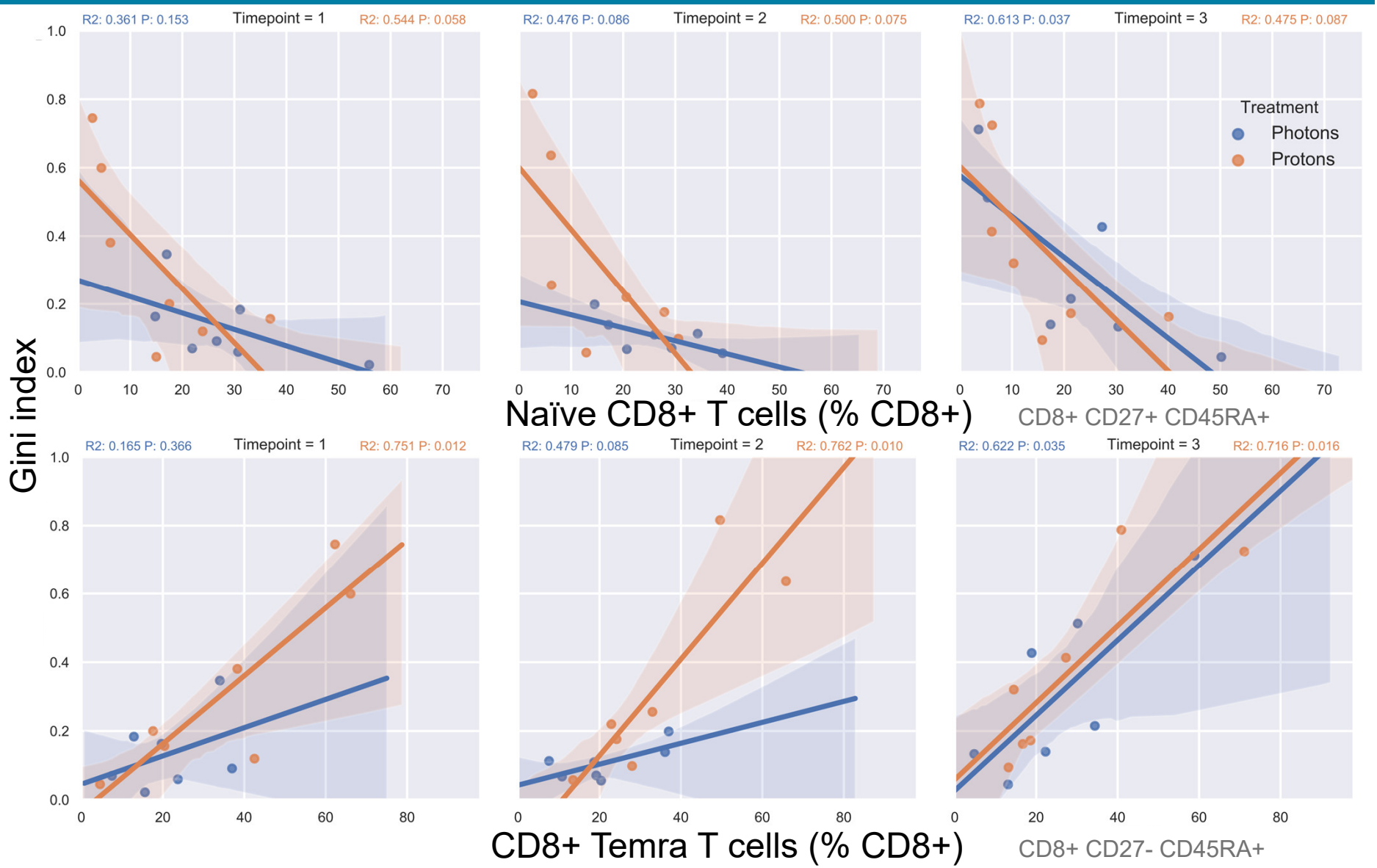
Decreased TCR retention in photon patients between timepoints



Increase in TCR inequality post-nadir negatively correlates with time to death post-recovery



Correlation between cytometric and repertoire parameters



Summary

- Photon based radiation therapy seems to induce a much more profound T cell compartment remodeling than protons
- Many of the changes brought photon-treated patient distributions into line with those of the (older but stable) proton-treated patient distributions
- Lymphocyte sparing radiation (e.g. using protons) may better synergise with immunotherapies

Acknowledgements

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