risk from LD-TBI and long-term HIV infection treated continuously with ART.

Results: Our modeling predicts that six fractions of combined LD-IR and aMTT would be needed to achieve a 95% probability of cure. Seven fractions would be needed for a 99% cure rate (see Table). RadRAT predicted an all-organ exposure of 25 cGy would have excess lifetime cancer risks of 5.02% and 3.76% above baseline risks of 43.95% and 46.1% for a 30-year-old female and male, respectively. Data from 2019 found LD-TBI (2 − 4.5 Gy in 1-2 fractions) with fludarabine had a twofold higher risk of subsequent malignant neoplasms than the general population. In comparison, 2015 data found the cancer risk for people living with HIV was elevated by a factor of 3.89 with a 95% confidence interval of 2.92-5.19.

Conclusion: Based on our analysis, the radiation-induced malignancy risk of LD-TBI compares favorably to the increased risk of cancer when living with HIV while on continuous ART. We recommend performing further research on LD-IR and given the mathematical feasibility of success, we are planning *in vitro* studies to evaluate the combination of LD-IR and aMTT to validate our assumptions.

Abstract 3425 − Table 1

	95% Cure Rate	99% Cure Rate
Latency Reversing Agent (log-efficiency)	5.8 log-kill	6.5 log-kill

Author Disclosure: **K. Doxsee**: Uncompensated; University of Florida College of Medicine. **S.C. Self**: Independent Contractor; Companion Animal Parasite Council. Grant/research funding; National Institutes of Health, US Heath Resources and Services Administration, Centers for Disease Control and d Prevention, the Duke Endowment, Prisma Health. Honoraria; Merck Corporation. Travel expenses; National Institutes of Health, US Heath Resources a. **P.J. Roth**: Clinical Faculty; University of South Carolina School of Medicine. **J.R. Henderson**: Partner; Quiverent LLC. Compensation/Payment; Prisma Health. Partnership; Quiverent. **J.M. Stenbeck**: Physics Advisory Position; Medical Dosimetry Certification Board. **C.M.G. Schammel**: Uncompensated; University of South Carolina School of Medicine Greenville. **J.T. Grier**: Grant/research funding; Prism Health ED Rsch Inst, National Institutes of Health. Advisor; Amer Society for Microbiology. **M.S. Shtutman**: Grant/research funding; University of South Carolina. Travel expenses; University of South Carolina. Salary support; University of South Carolina. involved in the organization; Society for NeuroImmune Pharmacology. **S.B. Weissman**: Chair of Subcommittee on Practice Standards and Guidelines; IDSA Practice Standards and Guidelines Subcommitttee Chair. **J.J. O'Connell**: Copyright/Patent/License/Royalty; Prisma Health and University of South Carolina. Treasurer; Holy Family Communications.

3426

Risk Factors for Lateral Pelvic Lymph Node Metastasis in Rectal Cancer

B. Aydin,[1] Ö. Duran Can,[2] S. Onder,[1] Ç. Duymaz,[1] T. Bisgin,[3] F. Barlık,[4] İ. Öztop,[5] S. Sokmen,[3] and İ.B. Gorken[1]; *[1]Dokuz Eylul University Department of Radiation Oncology, İzmir, Turkey, [2]Manisa Celal Bayar University Department of Radiation Oncology, Manisa, Turkey, [3]Dokuz Eylul University Department of General Surgery, İzmir, Turkey, [4]Dokuz Eylül University Department of Radiology, İzmir, Turkey, [5]Dokuz Eylul University Department of Medical Oncology, Institute of Oncology, İzmir, Turkey*

Purpose/Objective(s): This study aimed to assess the pre-treatment prevalence of lateral pelvic lymph node metastasis (LPLNM) in patients with rectal cancer and identify the associated risk factors.

Materials/Methods: We retrospectively evaluated 241 patients who underwent neoadjuvant chemoradiotherapy for rectal cancer between 2014 and 2024. All patients were staged using contrast-enhanced rectal MRI. The lower, middle, and upper rectum were defined as 0−5 cm, 5−10 cm, and 10−15 cm from the anorectal junction, respectively. Pelvic lymph nodes outside the mesorectum were considered metastatic if they had a short axis diameter of ≥1 cm or a diameter of 5−9 mm with at least two of the following MRI characteristics: heterogeneous signal intensity, round shape, or irregular borders. Mesorectal fascia involvement (MRFI) was defined as a tumor distance of ≤1 mm from the mesorectal fascia on MRI. Categorical and continuous variables were analyzed using the Chi-square (χ^2) test and the Mann-Whitney U test, respectively.

Results: Fifty-two LPLNMs were detected in 41 out of 241 patients (17%) with a median age of 63 years (range: 23−90). Among them, 35 patients (85.4%) had unilateral LPLNM, while 6 (14.6%) had bilateral involvement. The median number of LPLNMs was 1 (range: 1−7). The median short-axis diameter of metastatic lymph nodes was 11 mm (range: 7−20 mm). The distribution of LPLNMs sites was as follows: 22 (42.3%) internal iliac, 21 (40.4%) obturator, 7 (13.5%) common iliac, and 2 (3.8%) external iliac nodes. No statistically significant association was found between LPLNM and age ($p = 0.205$), gender ($p = 0.271$), pre-treatment CEA levels ($p = 0.589$), extramural venous invasion ($p = 0.580$), tumor growth pattern ($p = 0.994$) or tumor morphology on MRI ($p = 0.939$). However, LPLNM was significantly associated with larger tumor diameter ($p < 0.001$), an increased number of mesorectal lymph node metastases ($p = 0.033$), advanced T stage ($p = 0.041$), and tumor location ($p = 0.013$). The rate of LPLNM was significantly higher in tumors with MRFI compared to those without MRFI (26.3% vs. 12.2%, $p = 0.006$), in tumors ≥T3d compared to <T3d (28.3% vs. 14.3%, $p = 0.024$), in tumors involving both the lower and middle rectum compared to those not involving both regions (23.7% vs. 8.5%, $p = 0.002$). The risk of LPLNM was significantly associated with tumor differentiation, with rates of 7.6% (9/118) in well-differentiated tumors, 29.6% (16/54) in moderately differentiated tumors, and 77.8% (7/9) in poorly differentiated tumors ($p < 0.001$).

Conclusion: LPLNM was found to be significantly associated with larger tumor diameter, advanced T stage, an increased number of mesorectal lymph node metastases, involvement of both the lower and middle rectum, MRFI, and poorer tumor differentiation. These findings highlight the importance of comprehensive pre-treatment imaging assessment to identify high-risk patients who may benefit from intensified treatment strategies.

Author Disclosure: **B. Aydin**: None. **Ö. Duran Can**: None. **S. Onder**: None. **Ç. Duymaz**: None. **T. Bisgin**: None. **F. Barlık**: None. **İ. Öztop**: None. **S. Sokmen**: None. **İ.B. Gorken**: None.

3427

A Novel Tool to Predict Primary Tumor Location in the Setting of Metastatic Cancer with Unknown Primary

K. Eldeeb,[1] S. Badat,[2] H.K. Perlow,[3] A. Baydoun,[4] P. Vempati,[5] Y. Yang,[2] D.E. Spratt,[3] M. Wang,[2] and N.G. Zaorsky[3]; *[1]Case Western Reserve School of Medicine, Cleveland, OH, [2]University Hospitals, Case Western Reserve University School of Medicine, Cleveland, OH, [3]Department of Radiation Oncology, University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH, [4]Department of Radiation Oncology, University Hospitals Cleveland Medical Center/ Seidman Cancer Center, Cleveland, OH, [5]Northwell Health, Lake Success, NY*

Purpose/Objective(s): There is currently no reliable model that can predict the primary cancer location for patients with newly diagnosed metastatic disease. Our goal is to build a tool to predict the location of primary cancer in the setting of metastatic disease based on simple clinicopathologic covariates, including imaging, but without pathology or labs. We hypothesize that this tool would have higher accuracy than guess.

Materials/Methods: The Surveillance, Epidemiology, and End Results (SEER) database was used to include patients with metastatic disease from 2010-2020. Patients were randomly split into training (70%) and testing (30%) sets. A total of 26 primary sites were included. Multiple machine learning models, including a gradient boost and random forest model, were trained to predict the primary tumor site. Conventional models, such as random guess and weighted guess, were used for baseline comparison. Model performance was evaluated using top-K accuracy metrics, and accuracy was reported as the average and standard deviation based on 100 planning tool simulations.