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The Roach Equation: value of "old" clinical tools in the era of new molecular imaging

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In the July 2020 issue of *The Journal of Nuclear Medicine*, Koerber and colleagues present a single institution retrospective analysis of the incidence of nodal involvement in 280 men with newly diagnosed intermediate and (mostly) high risk prostate cancer who underwent prostate-specific membrane antigen (PSMA) PET/CT as a part of primary staging. These were pathologically validated by subsequent lymphadenectomy and the investigators compared the observed incidence of lymph node involvement (LNI) to the incidence predicted by the "Roach equation"(*1*) by comparing the sensitivity and specificity). The bottom line was that the results appeared to be virtually identical. However, as usual, things aren't quite that simple.

The Roach equation, first derived in the early 1990s, uses a simple equation derived from the Partin nomogram to estimate the risk of lymph node involvement in prostate cancer, as follows: LNI risk (%) = 2/3 x PSA + (Gleason score - 6) x 10(*2*,*3*). This was validated in a cross-institutional study of nearly 300 patients between 1987 and 1991, and subsequently this equation has been used in a number of major randomized clinical trials including RTOG 94-13(*4*) and RTOG 09-24 to evaluate the role of elective pelvic nodal irradiation in the definitive management of patients with prostate cancer. This is important because some studies suggest that prophylactic whole-pelvis radiotherapy (WPRT) may decrease treatment failure rates and improve biochemical-relapse free survival(*4*,*5*), though not necessarily disease-free or overall survival(*6*). However, whether there is a survival benefit added by elective pelvic nodal irradiation awaits the now fully accrued Phase III RTOG 09-24 which enrolled over 2500 patients with the goal of providing a definitive answer as to the degree of clinical benefit and toxicity of elective WPRT in men with intermediate-risk and high-risk prostate cancer.

However, the accuracy and clinical value of the Roach equation has been called into question. Some studies including several studies using institutional data and data from large cohorts such as the Surveillance, Epidemiology, and End Results (SEER) database, have reported that the Roach equation overestimates the risk of LNI (based on nodal findings at the time of prostatectomy)(*7*,*8*). This discrepancy is most likely due to underestimation of the rates of LNI in the setting of inadequate pelvic lymph node dissection. More recent studies in which all patients underwent extended PLND appears to confirmed the accuracy of the "Roach equation".(*9*)

Recent studies , PSMA PET and Fluciclovine F-18 PET studies have demonstrated the role of molecular imaging in physician decision making among patients with biochemical recurrence as well as in the upfront setting among patients with intermediate and high risk prostate cancer at the time of initial diagnosis. (*10*–*14*)

Indeed, Koerber et al showed that the Roach equation is a good predictor of the risk of LNI, with an average AUC of 0.781(*1*). This is on par with that historically reported by Abdollah et al, which showed an AUC of 0.803, between the Roach equation and findings based on extended PLND(*9*). Both with PSMA/PET and using the Roach equation, roughly 30% of patients had ILN at the time of staging, as might be expected for this cohort of which 84% had high risk disease. The authors suggest that based on these findings that the Roach equation is still of value in the current clinical era but that it tends to lean towards overestimation.

A number of limitations are important to consider in interpreting these findings, however. Perhaps most importantly, PSMA PET/CT, while highly specific (with most studies reporting rates >95%), has relatively limited sensitivity, with average sensitivity between 50-80% in most studies. The poor sensitivity is due to limits of detection and resolution using PET and CT imaging. For example, in the study by van Leeuwen et al., there was 0% sensitivity for lymph nodes under 2mm(*14*). It goes beyond saying that molecular imaging currently, and for the foreseeable future, will not be able to assess the risk of microscopic nodal metastases.
One might ask then what is the role for the Roach equation in the modern molecular imaging era and what is the role of imaging? We believe they are likely to be complementary. The "Roach equation" would appear to potentially be useful *in selecting* which patients should be offered such imaging, while the imaging can identify the sites of relatively bulky nodal disease, allowing these areas to be selectively targeted. Thus, for example at UCSF PET positive areas are given a higher (e.g. 60Gy+ in 25 fractions) doses than PET negative nodal drainage areas (e.g. 45 to 50 Gy).

Overall, we applaud the efforts made by Koerber and colleagues to examine how molecular imaging may affect the utility of conventional "old-fashion" clinical tools such as the Roach equation. Certainly, as molecular imaging and potentially genetic/molecular profiling continue to develop and make their way into the clinic, we must reassess how and which tools should be used in the diagnosis and management of prostate cancer patients. It is worth remembering that such studies as the PSMA PET are costly and the use of such tools as the "Roach equation" to assess the pretest probability of LNI may be helpful in determining which patients would likely to benefit from molecular imaging.

COI/Disclosures
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