Nature Reviews Urology **8**, 649 (2011); doi:10.1038/nrurol.2011.184

PROSTATE CANCER

PET–CT for pelvic node staging

[11C]choline PET–CT could be an effective and noninvasive method for identifying patients with high-risk prostate cancer who need pelvic radiotherapy. Following on from promising preliminary studies of [11C] choline PET, Contractor and colleagues have published data to show that a combined PET–CT multimodality imaging approach can further enhance the detection of pelvic lymph node metastases.

Node dissection is the current gold standard for pelvic lymph node detection, but it is invasive, lacks reliability, and has associated morbidity. Although MRI and CT offer alternatives, these investigations are less sensitive. However, PET can provide functional information relating to tissue activity, thus generating superior staging information.

Contractor *et al.* showed that [11C]choline PET–CT is both well tolerated—with no immediate or delayed complications—and associated with increased sensitivity (51.9%) compared to MRI (18.5%) and [11C] choline PET (40.7%). An improvement in diagnostic accuracy was particularly evident in detecting subcentimeter disease. "This [research] should enable the integration of [11C]choline PET–CT into radiotherapy planning: for example, dose escalation for nodal disease and selecting patients who do not need pelvic radiotherapy," says Eric Aboagye, who led the study.

However, an obstacle to the widespread use of [11C]choline PET–CT is the short half-life of the [11C] radioisotope (20.9 min), which requires an on-site cyclotron. To overcome this issue, [18F] analogues are being developed, with increased stability (half-life of 109.8 min) and specificity. "Our group has developed a more metabolically stable choline analogue—[18F]fluoromethyl-[1,2-2H4]-choline," Aboagye reveals. "The new radiotracer employs fluorine-18, the most clinically relevant radioisotope for PET. This novel radiotracer has improved stability and enhances the sensitivity of tumor imaging through increased substrate availability. It has been validated in preclinical models of cancer and is awaiting human studies, which are scheduled for 2012."

Importantly, the group also established a link between [11C]choline tumor uptake and expression of the choline kinase CHKα; a relationship which could be used to develop new targeted therapies. No correlation was identified between CHKα expression and tumor proliferation rate, suggesting that CHKα is a proliferation-independent marker of the prostate cancer phenotype. "Estimates of proliferation rate, described in terms of a potential Doubling Time (Tpot) show that prostate tumors have the longest Tpot of any human tumor ranging from 15 to more than 70 days with a median of 42 days," explains Aboagye. "It, therefore, did not really surprise us that CHKα expression didn't correlate with tumor proliferation. There was a suggestion of increased intensity of CHKα staining (expression) with increasing Gleason score in our study. However, this finding has to be confirmed in a larger study."

"One line of research we are pursuing is exploiting the proliferation-independent choline phenotype for therapy," Aboagye continues. "This aspect of our research is at the laboratory stage and is not yet ready for clinical trials. Our recent findings indicate that [11C]choline PET–CT will be a useful end point for monitoring the effectiveness of such therapy."

Meanwhile, the diagnostic accuracy of PET scanning continues to improve, powered by technological advancements in the field. "Through the integration of faster and brighter scintillators (such as lutetium oxyorthosilicate [LSO]), software advances, improved computing power, multimodality imaging (combined PET–CT or PET–MRI), and time-of-flight PET, this technology is maturing," Aboagye concludes. "These developments are taking place now and promise to further improve the sensitivity and spatial resolution of the reconstructed image."

Melanie Clyne

Original article Contractor, K. B. *et al.* Use of [11C]choline PET-CT as a non-invasive method for detecting pelvic lymph node status from prostate cancer and relationship with choline kinase expression. *Clin. Cancer Res.* doi:10.1158/1078-0432.CCR-11-2048

© 2011 Macmillan Publishers Limited. All rights reserved