PSMA PET/CT and MRI for Determining Focal Therapy Eligibility in Patients with Prostate Cancer: Cohort Study with Histopathologic Validation

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Purpose: To evaluate whether prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT), multiparametric magnetic resonance imaging (mpMRI), or their combination more accurately determines eligibility for focal therapy in patients with localized prostate cancer, using whole-mount histopathology after radical prostatectomy as the reference standard.

Materials and Methods: This retrospective single-center cohort study included patients who underwent both preoperative PSMA PET/CT and mpMRI within 6 months before radical prostatectomy between 2017 and 2024 and met biopsy-based criteria potentially compatible with focal therapy: ISUP grade group ≤3, unilateral disease on biopsy, and PSA <20 ng/mL. Blinded readers assessed each modality for extraprostatic extension, seminal vesicle invasion, bilateral disease, and multifocality. Focal therapy ineligibility was defined as any of these features on whole-mount histopathology. Diagnostic performance of PSMA PET/CT, mpMRI, and combined PET+MRI was compared using McNemar tests.

Results: Among 113 included patients, median age was 65 years and median PSA was 6.7 ng/mL. On biopsy, 4% had grade group 1, 27% had grade group 2, and 68% had grade group 3 disease; 69% were NCCN unfavorable intermediate risk. Whole-mount histopathology showed a high prevalence of exclusionary features, including extraprostatic extension in 53 patients (47%), seminal vesicle invasion in 18 (16%), bilateral disease in 48 (42%), and multifocal disease in 53 (47%). Overall, 90 patients (80%) were ineligible for focal therapy by histopathology. For the composite endpoint of focal therapy ineligibility, PSMA PET/CT showed sensitivity of 56.7% and specificity of 56.5%, while mpMRI showed sensitivity of 52.2% and specificity of 68.9%. Combined PET+MRI significantly improved sensitivity to 78.9% compared with PSMA PET/CT alone ($p<0.001$) and mpMRI alone ($p=0.008$), although specificity decreased to 26.1%. For individual features, mpMRI was more sensitive than PSMA PET/CT for extraprostatic extension (77.4% vs 35.8%, $p<0.001$), whereas PSMA PET/CT was more specific (86.7% vs 56.7%,

p<0.001). Adding PET to MRI improved sensitivity for multifocal disease and bilateral disease compared with MRI alone.

Conclusion: In this surgically validated cohort of patients who appeared potentially eligible for focal therapy based on biopsy criteria, most harbored exclusionary disease on whole-mount histopathology. Neither PSMA PET/CT nor mpMRI alone reliably identified focal therapy candidates. Combined PET+MRI substantially improved sensitivity for detecting ineligibility, supporting dual-modality imaging for pre-treatment focal therapy selection while acknowledging reduced specificity.