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A Prospective Within-Patient Comparison of Molecular Imaging Ligands for Detection Of Surgically Curable Primary Aldosteronism (PA), and an Assessment of Accuracy in Cortisol Co-Secretors

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Introduction: Molecular imaging could reduce the need for invasive, scarcely-available adrenal sampling (AVS) to identify aldosterone-producing adenomas (APAs). Easily-distributable ligands for widespread use will be needed. Imidazole ligands lacking selectivity *ex vivo* for CYP11B1 and CYP11B2 are rendered selective *in vivo* by pre-treatment with dexamethasone. **Aims** To determine whether post-dexamethasone para-chloro-2-[[1]⁸F]fluoroethyltomidate PET-CT (CETO) (T_{1/2} 110min), is interchangeable with previously validated [[1][1]C]-metomidate PET-CT (MTO) (T_{1/2} 20min) for the diagnosis of APA. To identify whether a non-fully-suppressed cortisol after prolonged (72h) low-dose dexamethasone forewarns of an increased risk of a false-positive MTO result, in the MATCH study cohort.¹ **Experimental design** Prospective within-patient comparison of diagnostic interventions (n=31), with independent scoring of each as high, medium, low probability of unilateral PA, blind to scoring of the other scan or AVS. Prospective measurements of cortisol after prolonged low-dose dexamethasone suppression (PLDDF) and urinary hybrid steroids, with 6-month post-operative PASO biochemical outcomes and APA somatic genotyping when high probability (MTO or AVS) mandated surgery. **Major results** MTO and CETO agreed in 29/31, kappa=0.85 [95%CI 0.68,1.00]. Scatter was evenly distributed on either side of zero on Bland-Altman analysis (bias -0.04, [95% CI -0.12,0.04]. Of all 174 MATCH-study patients (n=174) PLDDF was available in 156, 32 had PLDDF >25nmol/L. Of these, MTO scored 16 as high probability of unilateral PA, in whom there was complete PASO biochemical success in 14 (88%), and absent in 2 (12%), indicating possible false-positives (AVS had failed in both). In patients with PLDDF <=25nmol/L, MTO identified unilateral disease in 22, 19 (86.3%) of whom had complete biochemical success at 6 months, 3 (13.6%) with partial or absent success. 22 patients had both an elevated PLDDF and urinary hybrid steroid profiles measured, of whom 4 had an elevated 18OH/F ratio. PLDDF in unilateral and not-unilateral MTO outcome were comparable (unpaired T test p= 0.92). A known somatic genotype mutation was found in 21 patients with PLDDF >25nmol/l. PLDDF was highest in *KCNJ5* mutants (12/21, mean 55.3nmol/L), compared to *ATP1A1* (3/21, mean 44nmol/L), *CACNA1D* (4/21, mean 31nmol/L), *ATP2B3* (1/21, 36nmol/L) and *GNAQ* (1/21, 28nmol/L). All had complete biochemical success at 6 months post-op. **Conclusion:** CETO is interchangeable with MTO, which is non-inferior to AVS, in lateralising aldosterone excess in PA patients. False-positives rarely occurred by MTO, and autonomous cortisol secretion did not increase the chance of a false-positive MTO result, compared to patients without, in this cohort. **Reference:** (1) Wu X et al. *Nature Medicine*. 2023;29:190-202.

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