

Appendix 1***Additional details regarding ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) acquisition***

For ¹⁸F-FDG PET/CT image acquisition, patients fasted for 4–6 h and were encouraged to drink water *ad libitum*. Prior tracer administration, capillary blood glucose was verified and needed to be <150 mg/dL. To minimize physiologic muscular uptake, patients confirmed they had abstained from strenuous exercise during the preceding 24 h and remained quietly recumbent throughout the post-injection uptake period of generally one hour. An activity of ¹⁸F-FDG (dose weight-adjusted according to institutional standards) was injected intravenously, and imaging commenced 60±5 min thereafter.

A low-dose, non-contrast helical CT (tube voltage, 120–140 kV; tube current, 80–200 mA or mA automodulation; pitch, 1.375; time per rotation, 0.8 s; slice thickness, 3.75 mm) covering the base of skull to mid-thigh was acquired first to generate the attenuation map and provide anatomical correlation to the FDG images. Without changing patient position, three-dimensional PET emission data were then acquired over the identical field of view [2 min each (starting from the top of the skull and ending at the mid-thigh)]. PET datasets were corrected for attenuation, scatter, randoms, dead time and decay, followed by iterative reconstruction (OSEM, 4 iterations × 5 subsets, time-of-flight and point-spread-function modelling). Multiplanar (axial, coronal and sagittal) reformats were reviewed on a dedicated workstation (syngo.via, Siemens Healthineers, Erlangen, Germany).

Regarding the timing, the first PET-CT was performed one month before the initiation of the systemic therapy and the second one, 2 weeks before the surgery.

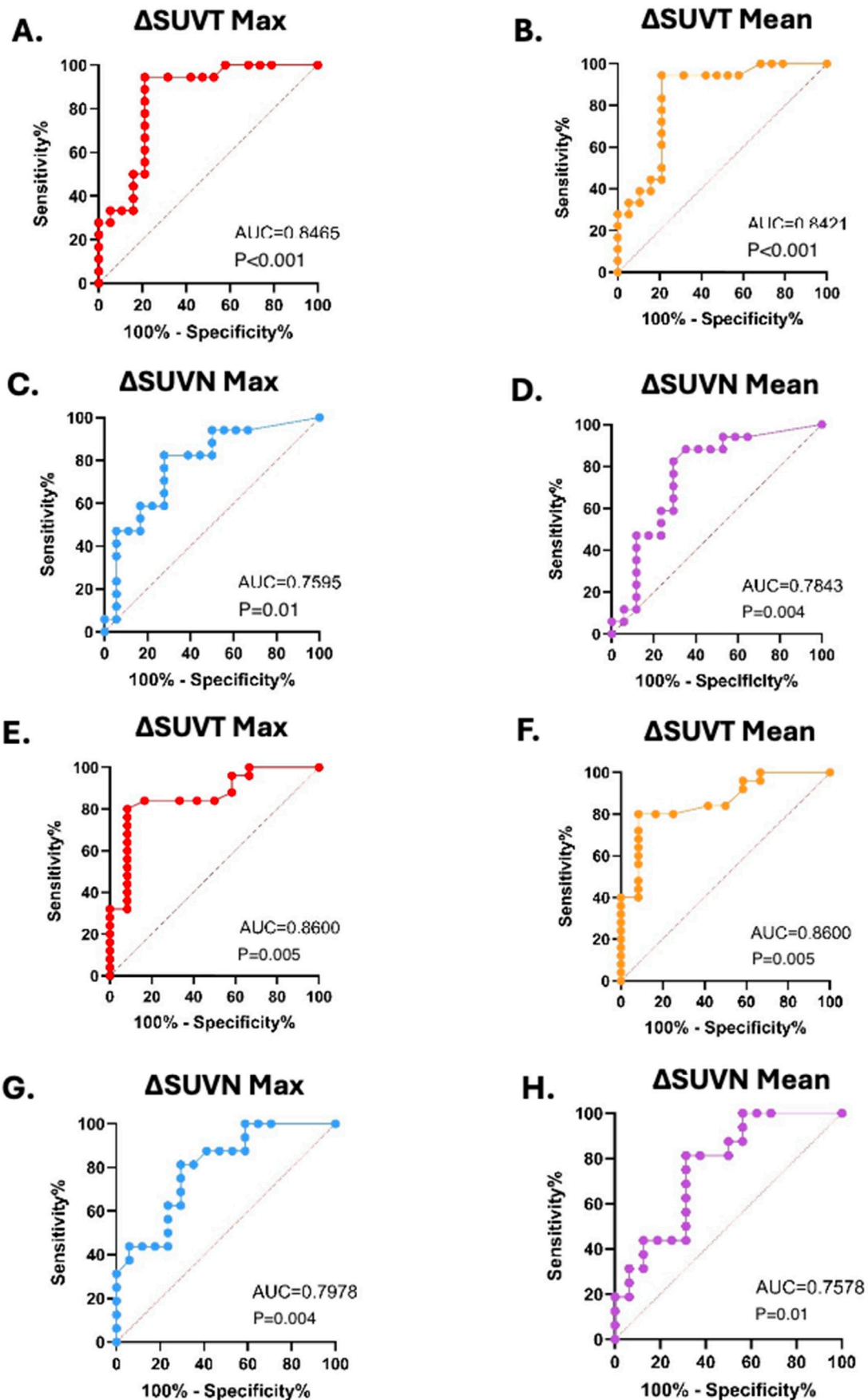


Figure S1 ROC analysis of SUV changes in primary tumor and associated lymph nodes for predicting pathologic downstaging. ROC curve analysis for Δ SUVT Max (A), Δ SUVT Mean (B), Δ SUVN Max (C) and Δ SUVN Mean (D) to predict MPR or pCR following induction therapy. ROC curve analysis for Δ SUVT Max (E), Δ SUVT Mean (F) to predict a downstaging from Tx to T0 and for Δ SUVN Max (G) and Δ SUVN Mean (H) to predict a downstaging from Nx to N0. AUC, area under the curve; pCR, complete pathologic response; ROC, receiver operating characteristic; SUV, standard uptake value; Δ SUVN Max, variation in the maximum SUV of lymph nodes; Δ SUVN Mean, variation in the mean SUV of the lymph nodes; Δ SUVT Max, variation in the maximum SUV of the primary tumor; Δ SUVT Mean, variation in the mean SUV of the primary tumor.