Shaw and colleagues* have reported on $\text{A}_\beta^{1\text{to}42}$ (and other biomarkers) for the detection of mild Alzheimer's disease (AD). Data describing the results of this test in a sample of 56 autopsy-confirmed people with AD and 52 cognitively normal (NC) people are reported in the figure on the next page. The authors constructed an ROC curve for $\text{A}_\beta^{1\text{to}42}$ and identified a cutpoint that yielded the greatest diagnostic test accuracy.

Whether or not you agree with the authors' methods, use the information in the figure to:

Q1. Divide the $\text{A}_\beta^{1\text{to}42}$ data into 3 strata (<130, $\geq 130$ to $< 185$, and $\geq 185$), create the necessary $\text{A}_\beta^{1\text{to}42}$ 2x2 tables, and plot the ROC curve that summarizes this multiple outcome test. Note: the strata you are being asked to use are defined by the solid vertical lines, NOT the dashed vertical line. See bottom of figure for information about observations that appear to touch the lines or that overlap each other. Assume that the 52nd normal observation lies in the lower right corner of the figure ($\text{A}_\beta^{1\text{to}42} > 200$ and Tau <90).

Q2. If you are making a treatment decision for an older person for whom the pre-test probability of AD is 0.12 and $\Delta \text{OD}^+ = 0.75 \Delta \text{OD}^+$ (i.e., the ratio of differences in outcomes is 0.75) which cut-off would you use for a positive test? What is the resulting post-test probability of disease?

Q3. If the pre-test probability was 0.26 and the ratio of the differences in outcomes was unchanged, which cut-off would you use?

OPTIONAL: (Assuming the test were costless,) what is the lowest pre-test probability where you should first consider withholding the test and treating empirically (i.e., treat all test results as positive)?

Please show your work and report results to 3 decimals.

Plot of cerebrospinal fluid (CSF) tau concentration versus CSF amyloid-B 1 to 42 peptide ($\text{AB}_{1-42}$) concentration for 56 autopsy-confirmed (AD) cases (solid circles) and 52 elderly cognitively normal (NC) subjects (open circles). Vertical lines added at $\text{AB}_{1-42}=130$ and $\text{AB}_{1-42}=185$. NOTE: In addition to the 5 visible partially overlapping open circles with $\text{AB}_{1-42}>200$, consider one additional open circle in this region to represent 2 cases.