The present study assessed the diagnostic accuracy of 16-row MSCT-CA using 2 protocols for image visualization: the first protocol was based on a standard series of projections that the observer could assess using a workstation implemented in a digital archiving system. The second protocol required the interaction between the operator and the dataset using a 3-dimensional workstation equipped with all available postprocessing tools. The results show that an approach using standard projections prepared by a technician was faster. In addition, it was probably less expensive, in that image processing was performed by a radiographer and image assessment by a radiologist. However, the standard projections approach had a significantly lower diagnostic sensitivity compared with the interactive postprocessing. In particular, the proximal segments, where disease was more frequent and of greater clinical importance (the proximal left anterior descending artery alone represented of significant lesions), were the sites that showed a major and significant discrepancy between the techniques. This reflects the large number (37 of 92; 40%) of lesions that were missed using standard projections. Specificity, instead, did not differ significantly between techniques.

One limitation of our study is that patients were retrospectively enrolled and selected. Patients with severe residual motion artifacts were not enrolled. This can improve the overall diagnostic accuracy. The results cannot be extrapolated to other patient populations, such as those with stents or bypass grafts. Finally, our interactive postprocessing protocol is based on a single vendor platform.

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Prediction of Heart Transplant Rejection With a Breath Test for Markers of Oxidative Stress

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The Heart Allograft Rejection: Detection with Breath Alkanes in Low Levels study evaluated a breath test for oxidative stress in heart transplant recipients, and we report here a mathematical model predicting the probability of grade 3 rejection. The breath test divided the heart transplant recipients into 3 groups: positive for grade 3 rejection, negative for grade 3 rejection, and intermediate. The test was 100% sensitive for grade 3 heart transplant rejection when the p value was ≥0.98, and 100% specific when the p value was ≤0.058; in the intermediate group, the breath test determined the probability of grade 3 rejection and the predictive value of the result.

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*Dr. Phillips is president of Menssana Research, Inc. and holds patents issued and pending on the breath test employed in this study.

We have reported a breath test for oxidative stress[1] that identified grade 3 rejection in heart transplant recipients in the Heart Allograft Rejection: Detection with Breath Alkanes in Low Levels (HARDBALL) study.[2,3] We report here a follow-up analysis of the results of the HARDBALL study in which we determined the sensitivity, specificity, and predictive value of the breath test as a marker of grade 3 heart transplant rejection.

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We employed a breath collection apparatus to collect 1,061 breath samples from 539 heart transplant recipients before endomyocardial biopsy over a 3-year period at 7 medical centers. Volatile organic compounds in breath and room air were analyzed by gas chromatography and mass spectroscopy, and the breath methylated alkane contour (BMAC), a 3-di-

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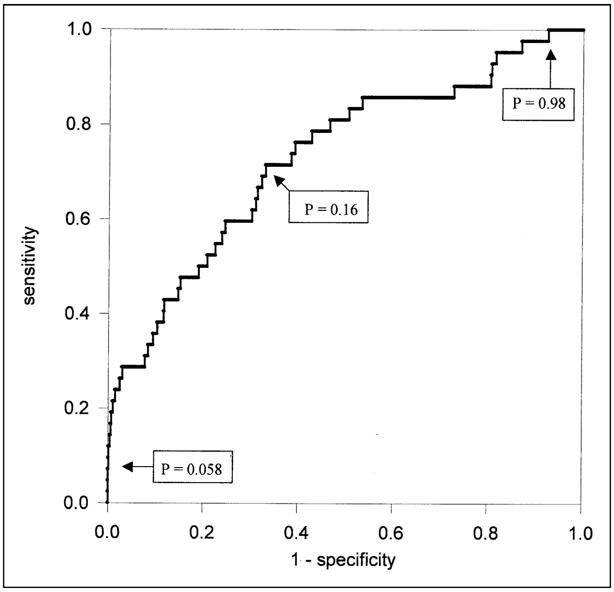

FIGURE 1. Receiver-operating characteristic of breath test for grade 3 heart transplant rejection. The breath test was 100% sensitive for grade 3 heart transplant rejection when the predicted p valie was ≥0.98. Specificity was 100% when the predicted p value was ≤0.058. At the shoulder of the curve (predicted p = 0.16), the sensitivity was 71.4% and the specificity was 62.4%.

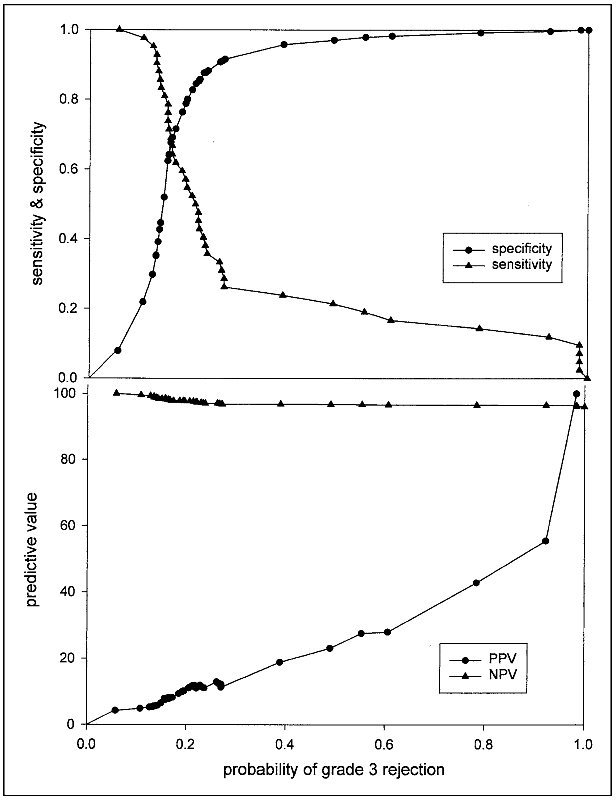

FIGURE 2. Variation in sensitivity, specificity, and predictive value of the breath test. This figure demonstrates the variation in sensitivity and specificity *(upper panel)*) and positive (PPV) and negative predictive values (NPV) *(lower panel)* of the breath test, depending upon the predicted probability of grade 3 rejection. The PPV of the breath test for grade 3 rejection (i.e., its ability to rule in grade 3 rejection) increased to 100% when the predicted probability was ≥0.98. However, the NPV of the breath test (i.e., its ability to rule out grade 3 rejection) showed less variation because of the low prevalence of the disorder.

mensional display of the abundance of C4-C20 alkanes and monomethylated alkanes was constructed for every patient.[1] The institutional review boards of all participating institutions approved the research.

BMACs in heart transplant recipients with grades 0, 1, and 2 rejection were compared with those with grade 3 rejection using forward stepwise discriminant analysis, employing maximal significance of F to enter (0.15) and minimum significance of F to remove (0.20). The resulting mathematical model generated a value from each patient's BMAC ranging from 0 to 1.0, indicating the probability of grade 3 rejection. Cross validation of the patient's classification was performed with a "leave 1 out" discriminant analysis procedure, which predicted whether the patient belonged to the group with grade 0, 1, or 2 rejection or the group with grade 3 rejection. The predicted probability of grade 3 rejection was evaluated as a marker of disease by determining its sensitivity and specificity (shown in a receiver-operating characteristic curve in Figure 1) and its positive predictive and negative predictive values (Figure 2).

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These findings demonstrate that the breath test divided the heart transplant recipients into 3 groups: positive for grade 3 rejection, negative for grade 3 rejection, and intermediate. In clinical practice, results in the intermediate group could be reported as the probability of grade 3 rejection, with the positive or negative predictive value of the test, dependent upon whether the p value was >0.5 or <0.5.

Breath testing provides a noninvasive new test for grade 3 heart transplant rejection that could potentially reduce the number of endomyocardial biopsies performed and consequently reduce patient morbidity and health care costs.

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