Obstructive sleep apnea (OSA) is a common clinical condition affecting 2 to 4% of middle-aged women and men. It can lead to numerous complications including decreased quality of life, reduced occupational performance, and increased risk of a motor vehicle accident. When untreated, significant OSA is associated with increased mortality largely due to cardiovascular causes. The diagnosis of OSA or, more precisely, OSA syndrome requires the presence of symptoms and an elevated apnea plus hypopnea index (AHI). The threshold of AHI beyond which OSA is diagnosed is usually between 10 and 20 obstructive events per hour of sleep recorded during nocturnal polysomnography (PSG).

Previous efforts to develop a clinical screening or case-finding instrument for the diagnosis of OSA have been based on patient questionnaires usually combined with anthropometric and physical findings. These studies have used a wide variety of statistical approaches and techniques to predict the presence of OSA. These approaches have been limited by poor sensitivity or less-than-optimal specificity (even when sensitivity has been high), by


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conflicting results between the different studies, and by the lack of prospective validation in some of the models that hinders their generalizability. It is noteworthy that the overall subjective impression of experienced sleep physicians correctly identifies about 50% of the patients with OSA.\textsuperscript{8,9} Portable home sleep monitoring has also been proposed for the diagnosis of OSA. The potential benefits of home sleep monitoring include reduced costs and the ability to evaluate patients in their usual environment. Potential disadvantages include the problems inherent in unattended monitoring (especially if the patient sets up the equipment) and the time and expense involved if a technician is required to instrument the patient at home. In the latter situation, there may be minimal financial savings over in-laboratory PSG. In addition, many of the home monitoring systems that are available have not been adequately validated. PSG is therefore the diagnostic standard for OSA due to the lack of well-validated clinical or other screening tools. PSG may be expensive and inconvenient for the patient, and it is a labor-intensive, specialized procedure that may have limited accessibility in many jurisdictions. Increasing awareness of the adverse health effects of OSA and the availability of effective therapies have led to increased demand for PSG and, concomitantly, concerns by health insurance providers about increased expenditures for the diagnosis and treatment of OSA.

Artificial neural networks (ANNs) are computer programs modeled after the biological nervous system, and they are capable of recognizing complex patterns in data based on experience. Their application is useful in complex problems because they can analyze a large number of linear and nonlinear variables without the operator knowing or making assumptions about the relationships between the variables. Neural networks are “trained” by presenting a set of data together with the outcomes that the trainer wishes the network to learn. The trained neural network can then be evaluated by inputting similar, but previously unseen, data. This artificial intelligence approach for outcome prediction has been used successfully in other medical applications, including the prediction of acute myocardial infarction in patients presenting to an emergency room physician,\textsuperscript{14} the diagnosis of pulmonary embolism,\textsuperscript{15,16} and the predicted length of ICU stay.\textsuperscript{17} ANNs have been shown to outperform physician impression or prediction\textsuperscript{15,19} and to equal or exceed traditional statistical modeling in the prediction of outcomes.\textsuperscript{20,21} This study was conducted to test the hypothesis that a trained generalized regression neural network (GRNN) could accurately classify patients with OSA from clinical data.

### Materials and Methods

The clinical data were collected from a retrospective review of randomly selected patients who presented to the London Health Sciences Center Sleep Clinic for assessment of possible OSA and who went on to have PSG. Greater than 95% of patients referred for possible OSA have PSG performed in their work-up. Reasons for not going on to PSG included a clinical diagnosis other than OSA (eg, insomnia or sleep-related laryngospasm) and patient refusal. Excluded from the study were patients < 16 years of age, patients with a nondiagnostic study (eg, total sleep time < 2 h), and patients referred for split-night studies. The latter group was comprised largely of patients with morbid obesity and obesity/hypoventilation (hypoxemia and hypercapnia), and the clinical likelihood was so great and the symptoms so severe that the diagnostic and therapeutic studies were combined in order to implement therapy as quickly as possible.

#### Overnight PSG

PSG was performed on 1 night in all patients. The sleep study montage included EEG (C3/A2, C4/A1, O2/A1), electro-oculogram, submental electromyogram, left and right anterior tibialis electromyogram, ECG, thoracoabdominal motion, oronasal airflow (expired CO\textsubscript{2}), and arterial oxygen saturation with pulse oximetry using an ear probe sensor. The studies were scored manually, and the total AHI (number per hour total sleep time) was calculated for the night. Obstructive apneas were defined as the cessation of airflow for at least 10 s accompanied by ongoing respiratory effort. Obstructive hypopneas were defined as a reduction in airflow of at least 50% for at least 10 s accompanied by a reduction in respiratory effort and by an arousal or an arterial oxygen desaturation of at least 3%. OSA was defined as an AHI ≥ 10/h for the purposes of this study.

#### Clinical Data

Forty-five clinical variables from nine categories were recorded in the database. These variables were chosen on the basis of previously published screening studies\textsuperscript{7-13} and clinical experience. The categories included demographics (age, gender, marital status); nocturnal symptoms (frequent awakenings, choking, gasping); bed partner observations (snoring, witnessed apnea, observed choking, restlessness); daytime symptoms (unrefreshing sleep, morning headache, reported excessive daytime sleepiness, Epworth sleepiness scale, impaired nasal breathing); past medical history (nasal trauma, hypertension, airway surgery, allergies); medications (sedative/hypnotics, antidepressants, antihypertensives); social history (alcohol consumption, smoking history and pack-years); and anthropometrics (weight, height, body mass index [BMI] in kg/m\textsuperscript{2}, neck circumference [NC]). Alcohol consumption was categorized as none, mild (up to 1 drink per day), and moderate to heavy (> 2 drinks per day). Data from the physical examination included systolic and diastolic BP, nasal obstruction, tonsillar enlargement, soft palate and/or uvular enlargement, crowding of the posterior oral pharynx, and the presence and grade of maxillary overjet. Data values that were not available in the chart review were obtained, whenever possible, by calling the patients by telephone or at a follow-up clinic visit. Less than 1% of the numeric data values were missing from the database. Missing numerical values (eg, NC) were recorded as the mean value from the group the subject was in (eg, women). Missing categorical values were recorded as negative.

GRNN software was used (NeuralShell Classifier Version 2; Ward Systems Group; Frederick, MD). Data preprocessing was conducted prior to neural network training to reduce the number of...
of input variables to an optimal number of more discriminating factors. The raw data were first divided into two subsets according to AHI (i.e., AHI < 10 and AHI ≥ 10). Differences between the subsets were then assessed using Student’s t test for each of the parametric variables and the Mann-Whitney U test for the nonparametric variables. Categorical variables were compared by χ² testing. All analyses were performed using appropriate software (Microsoft Excel Version 5.0 for the Macintosh; Microsoft; Redmond, WA and Systat Version 5.2 for the Macintosh; SPSS; Chicago, IL). A p value ≤ 0.1 was arbitrarily chosen as the cutoff for the continued inclusion of a given variable in the final model.22–25 The 45 clinical variables were reduced to 23 variables by data preprocessing. For the purpose of ANN training, the preprocessed database (n = 405) was randomly divided into a "training" set of 255 patients and a "test" set of 150 patients. During training of the network, the training set was repeatedly presented to the network until 99.6% of the patients were learned. The test set of previously unseen cases was then presented to the trained network, and predictions were compared with actual outcomes.

The aim of this study was to predict those subjects who had OSA (i.e., AHI ≥ 10 from PSG). The accuracy, sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) were calculated. Accuracy was defined as the number of times the ANN correctly classified the patient as having or not having OSA.

**Results**

The prevalence of OSA (defined as AHI ≥ 10) in this series was 69% (53% in women and 76% in men). The demographic and clinical features of the study population are outlined in Table 1. There were more men than women in the data set, and on average the patients were middle aged and overweight. The prevalence of OSA in the training set and the test set were 72% and 65%, respectively (p > 0.05). There were small differences between the training set and the test set. The subjects in the test set had a larger BMI (p = 0.009) and a higher systolic BP (p = 0.002). There were proportionately more women in the test set (p = 0.03), and overall, more subjects were noted to have observed choking in the test set (p = 0.016).

**Patients With and Without OSA**

The differences between patients with and without OSA status are summarized in Table 2. Men were more likely to have OSA than women, and the patients with OSA were older and heavier with larger NCs and BMIs than patients without OSA. A history of observed choking and witnessed apneas was associated with the presence of OSA. The patients with OSA were more likely to drink alcohol and were more likely to be smokers. The patients with OSA were more likely to have a history of hypertension, and on physical examination their systolic BP was higher (136 ± 15.9 vs 127 ± 15.8 mm Hg; p ≤ 0.0001).

### Table 1—Patient Demographics and Clinical Features*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total n = 405</th>
<th>Training Set n = 255</th>
<th>Test Set n = 150</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>293</td>
<td>194</td>
<td>99</td>
</tr>
<tr>
<td>Female</td>
<td>112</td>
<td>61</td>
<td>51</td>
</tr>
<tr>
<td>Age, yr</td>
<td>47.2 ± 11.2 (20 – 79)</td>
<td>47.5 ± 11 (20 – 72)</td>
<td>46.9 ± 11.6 (23 – 79)</td>
</tr>
<tr>
<td>BMI, kg/m²†</td>
<td>31.5 ± 6 (16.6 – 54)</td>
<td>30.9 ± 5.5 (16.6 – 49)</td>
<td>32.6 ± 6.3 (22 – 54)</td>
</tr>
<tr>
<td>NC, cm</td>
<td>42.1 ± 4 (30 – 53)</td>
<td>42.0 ± 3.9 (30 – 53)</td>
<td>42.2 ± 4.1 (32 – 53)</td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic snoring</td>
<td>403 (99.8)</td>
<td>255 (100)</td>
<td>149 (99.3)</td>
</tr>
<tr>
<td>Observed choking†</td>
<td>190 (47)</td>
<td>108 (42.4)</td>
<td>82 (54.7)</td>
</tr>
<tr>
<td>Witnessed apneas‡</td>
<td>319 (79)</td>
<td>199 (78)</td>
<td>120 (80)</td>
</tr>
<tr>
<td>Hypertension‡</td>
<td>124 (30.6)</td>
<td>52 (20.4)</td>
<td>72 (48)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>149 (37)</td>
<td>85 (33.3)</td>
<td>64 (42.7)</td>
</tr>
<tr>
<td>Mild</td>
<td>190 (47)</td>
<td>126 (49.4)</td>
<td>64 (42.7)</td>
</tr>
<tr>
<td>Moderate to heavy</td>
<td>66 (16)</td>
<td>44 (17.3)</td>
<td>22 (14.6)</td>
</tr>
<tr>
<td>Smoking, pack-yr</td>
<td>15 ± 16.9 (0 – 90)</td>
<td>14.3 ± 16.6 (0 – 90)</td>
<td>16.2 ± 17.5 (0 – 90)</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>11 ± 4.9 (0 – 24)</td>
<td>10.8 ± 4.9 (0 – 24)</td>
<td>11.3 ± 4.8 (0 – 22)</td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>29.2 ± 28 (0 – 146)</td>
<td>27.7 ± 25 (0 – 146)</td>
<td>32 ± 33 (0 – 146)</td>
</tr>
<tr>
<td>Clinical score†</td>
<td>6.5 ± 2.1 (0 – 11)</td>
<td>6.2 ± 1.2 (3 – 9)</td>
<td>7.1 ± 3 (3 – 11)</td>
</tr>
<tr>
<td>Physical examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft palate enlargement</td>
<td>320 (79)</td>
<td>208 (81.6)</td>
<td>112 (74.7)</td>
</tr>
<tr>
<td>Crowded oral pharynx</td>
<td>315 (78)</td>
<td>202 (79.2)</td>
<td>113 (75.3)</td>
</tr>
</tbody>
</table>

*Date are given as mean ± SD (range) or frequency (%).
†p ≤ 0.05 for comparisons between the training and test set.
‡p ≤ 0.0005 for comparisons between the training and test set.
The patients with OSA were also more likely to have a large soft palate and crowded posterior oral pharynx. Patients with OSA were more likely to report moderate to severe excessive daytime sleepiness (47.7%) than patients without OSA (27.4%; \( p < 0.001 \)), although there was no difference in the Epworth Sleepiness Scale.

**Men and Women With OSA**

The differences between women and men with OSA are summarized in Table 3. The women were heavier (a larger BMI), but the men had larger NC. The men with OSA were more likely to be moderate to heavy drinkers than the women with OSA. Witnessed apneas were more common in the men with OSA than in the women with OSA.

**GRNN Prediction**

The 23 variables used in the neural network are listed in Table 4. A total of 255 training cases were used with a test set of 150 patients. Overall, the trained network had a mean predictive accuracy of 91.3% (95% confidence interval [CI], 86.8 to 95.8). The sensitivity of neural network prediction for the presence of OSA was 98.9% (95% CI, 96.7 to 100), and specificity was 80% (95% CI, 70 to 90). The PPV that the patient would have OSA if the network said so was 88.1% (95% CI, 81.8 to 94.4), whereas the NPV that the patient would not have OSA (if so classified) was 98% (95% CI, 94 to 100). The ANN misclassified one subject in the test set as not having OSA who had an AHI of 10; this subject had mild OSA with an AHI of 10.5. The ANN classified 12 subjects without OSA as having OSA. The area under the receiver operating characteristic curve was 0.94.

**Discussion**

We have shown in this retrospective study of a population of OSA patients that a trained GRNN can accurately diagnose the presence of OSA (defined as AHI \( \geq 10 \) events/h). To our knowledge, this study is the first use of a neural network to predict the presence or absence of OSA. The prevalence of OSA in this population was 69%, with OSA more common in men than in women. In the overall group, the presence of OSA was associated with a history of witnessed apneas, observed choking, and increased smoking and alcohol intake. The patients with OSA were more obese, had a higher BP, and were more likely to have a large soft palate and a crowded posterior oral pharynx. Different from some previ-
ously published studies\textsuperscript{7,8,11} yet compatible with others,\textsuperscript{9} reported excessive daytime sleepiness was associated with the presence of OSA.

OSA is an ideal condition for this use of screening or case-finding techniques. OSA is a chronic condition that is highly prevalent in the general population, and many effective therapies are available. If this neural network retains the high level of accuracy with prospective validation, it could be used as a simple clinical screening tool to reduce the number of PSG studies performed in patients without OSA.

The novel approach of applying a neural network to the clinically based prediction of OSA allows the incorporation of a much larger number of variables than what are conventionally used in linear or logistic regression techniques. Perhaps more important than the variables themselves is the technique of processing that seeks to identify subtle patterns and relationships. The user is shielded from the multitude of calculations, the technique is not cumbersome, and the prediction is free from bias, fatigue, and personal opinion. In addition, a well-trained neural network can easily handle differences between groups (e.g., between men and women) within the same model.

Screening tests are generally designed to favor high sensitivities so that cases are not missed. The development of clinical prediction rules emphasizing optimal sensitivity can be developed by accepting a concomitant decrease in specificity. The financial impact of varying the cutoff points is related to the costs (both financial and human) associated with false positive vs false negative results. Most previous clinical screening studies have attempted to rule in the presence of OSA with a high level of sensitivity in order not to miss significant OSA. When Hoffstein and Szalai\textsuperscript{9} studied 594 patients referred for possible OSA, they found that several variables from the history and physical examination were predictors of the presence of OSA (age, gender, BMI, witnessed apneas, pharyngeal examination). However, physician subjective impression only correctly identified 51% of the patients with OSA and 71% of the

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|}
\hline
Variables & Men & Women \\
\hline
Demographics & & \\
Age, yr & 48.3 \pm 10.5 (24 – 74) & 49.4 \pm 11.8 (20 – 79) \\
Body mass index, kg/m\textsuperscript{2} & 32 \pm 5.2 (21.8 – 54) & 36.5 \pm 6.5 (22.9 – 51) \\
NC, cm & 44 \pm 3.2 (37 – 53) & 39.7 \pm 3.3 (34 – 49) \\
Clinical features & & \\
Chronic snoring & 222 (100) & 59 (100) \\
Observed choking & 133 (60) & 38 (64.4) \\
Witnessed apneas\textsuperscript{†} & 199 (89.6) & 46 (78) \\
Hypertension & 85 (38.3) & 22 (37.3) \\
Alcohol consumption\textsuperscript{‡} & & \\
None & 57 (25.7) & 36 (61) \\
Mild & 113 (51) & 21 (35.6) \\
Moderate to heavy & 52 (23.4) & 2 (3.4) \\
Smoking, pack-yr & 17.7 \pm 18.8 (0 – 90) & 13.1 \pm 16.7 (0 – 55) \\
AHI, events/h & 40.6 \pm 26.9 (10 – 146) & 38.4 \pm 29.1 (11 – 127) \\
Clinical score\textsuperscript{‡} & 7.1 \pm 1.7 (3 – 11) & 8.1 \pm 1.9 (4 – 11) \\
Physical examination & & \\
Soft palate enlargement & 201 (90.5) & 52 (88) \\
Crowded oral pharynx & 208 (93.7) & 54 (91.5) \\
\hline
\end{tabular}
\caption{Patient Demographics and Clinical Features of Men and Women With OSA (AHI > 10)*}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
Variables & Characteristics \\
\hline
Demographics & Age, gender \\
Nighttime symptoms & Frequent awakening, experienced choking \\
Bed partner observations & Witnessed apneas, observed choking \\
Daytime symptoms & Reported excessive daytime sleepiness, Epworth sleepiness scale \\
Past medical history & Hypertension \\
Social history & Alcohol consumption, smoking in pack-yr \\
Anthropometrics & Height, weight, BMI, systolic BP \geq 140, diastolic BP \geq 90 \\
Physical examination & Tonsillar enlargement, soft palate enlargement, crowding of the oral pharynx \\
Clinical score & Sum of the clinical scores for the binary categorical values (maximum score = 12) \\
\hline
\end{tabular}
\caption{Patient Demographics and Clinical Features Used in the Neural Network of Prediction of OSA}
\end{table}
patients without OSA (sensitivity, 60%; specificity, 65%). They concluded that clinical impression alone could not reliably identify patients with or without OSA.

Crocker and colleagues\(^7\) used a logistic regression model developed with clinical variables to predict the presence of OSA. They found that age, witnessed apneas, BMI, and hypertension were independently associated with the presence of OSA (AHI > 15/h) in a group of 100 patients. The model had a sensitivity of 92% and a specificity of 51% for the diagnosis of OSA. The prevalence of OSA was only 27% in the initial group and 34% in the prospective test group of 105 patients. In the test group, 33 of 36 patients were correctly classified with OSA. The three patients in the test group who the model misclassified as not having OSA all had an elevated AHI > 40/h. The researchers estimated that they could reduce the number of PSG studies performed by approximately one third, but would have misclassified patients with significant OSA as not having OSA. Viner and coworkers\(^8\) developed a logistic regression model in 410 patients; age, gender, BMI, and snoring were retained as significant variables in the model. The prevalence of OSA was 46% in this population. The sensitivity was 94% and the specificity was 28% for the diagnosis of OSA (defined as AHI > 10). The area under the receiver operating characteristic curve was 0.77. The physician’s subjective impression of the presence of OSA had a sensitivity of 52% and a specificity of 70% with an accuracy rate of 63%. The application of this model would have allowed them to potentially reduce the number of PSG studies by one third. This model was not prospectively validated. The merits of these two different models are difficult to compare, as the prevalence of OSA in the populations studied were different and relatively low, and this affects the PPV and NPV of the test. The neural network, however, had better sensitivities for the diagnosis of OSA than either of these models, it had better specificities, and it did not miss cases of significant OSA while potentially reducing the number of PSG studies required.

Flemons and colleagues\(^11\) evaluated 180 patients with possible OSA, and they developed a model that included NC, hypertension, habitual snoring, and witnessed gasping or choking. The prevalence of OSA was 45% in the group (AHI > 10/h). Likelihood ratios were determined, and the calculated clinical score from the model was used to provide a posttest probability of OSA. This model was superior to physician impression, and it was comparable or superior to previously published models.\(^7,8\) Pradhan et al\(^13\) conducted a prospective study of OSA prediction in 150 patients. They adjusted the cutoff values in the clinical model (containing age, gender, loud snoring, and BMI) to have a sensitivity of 100% for the diagnosis of OSA. The prevalence of OSA was 57% (AHI > 10/h). They also developed a model that included overnight home oximetry. They found that it was more cost effective to pursue a clinical screening strategy than a clinical strategy with oximetry. The use of oximetry would have decreased the number of PSG by 13%, compared to an 8% reduction for clinical screening alone, but this savings was eliminated by the additional cost of home monitoring. Séries and colleagues\(^26\) used a qualitative analysis of home oximetry for screening in 240 patients referred for assessment of OSA. They reported a sensitivity of 98% and a specificity of 48% (PPV, 61%; NPV, 97%) in a population with a prevalence of 46%. The two patients who were misclassified as not having OSA had very low AHI (14/h and 16/h, respectively). Oximetry had a high sensitivity for the diagnosis of OSA in that study and could have reduced the number of PSG studies performed by approximately 25%. However, it is more time consuming and expensive to organize and interpret a home study than it is to use a simple clinical prediction model such as a neural network in the office setting.

This study differs from other screening studies because of the use of the neural network. If the neural network could accurately rule in or rule out OSA, then the PSG could be eliminated from the diagnostic assessment of some non-OSA patients, thereby saving valuable resources, potentially from some OSA subjects who might proceed to a therapeutic study (continuous positive airway pressure trial) instead of a diagnostic study. Given that OSA has significant consequences, physicians would not want to use a screening tool that missed patients with significant sleep-disordered breathing. In this study, the sensitivity for the diagnosis of OSA was 98.9% (95% CI, 96.7 to 100). The most important measure of the neural network as a screening instrument is the high sensitivity coupled with the low false-negative rate. The neural network misclassified only 1 out of 150 cases as not having OSA when the AHI was ≥10/h. This subject had an AHI of 10.5 events per hour, a very low level of OSA. This suggests that the neural network does not miss serious cases of OSA when it does make a mistake. Only 12 cases without OSA were classified as having OSA and therefore underwent potentially unnecessary PSG testing. Overall, 48 patients (32%) would not have required PSG based on the neural network prediction. Although a specific cost analysis was not performed in this study, it is apparent that the number of PSG studies could be reduced if the network could accurately rule in and rule out OSA. These patients could have been reassured that they did not have significant OSA; potentially, they could have proceeded directly to treatment based on their risk...
factors and symptoms. Ultimately, this approach may increase the number of patients evaluated for the possibility of OSA, while reserving PSG for patients who are more likely to have significant sleep-disordered breathing. In centers with long waiting lists, this could also reduce waiting times for evaluation.

The limitations to this study include the retrospective nature of the data review, the lack of prospective validation, and the relatively small numbers. The model performed exceedingly well, even with the small numbers; however, in general, the performance of neural networks improves with increases in the size of the data set. Future work with this prediction technique will include expansion of the training set and validation in a larger set of consecutively and prospectively collected cases. This model was developed in a population with a fairly high prevalence of OSA (Referral to a sleep clinic; prevalence, 69%), and it needs to be tested in a population with a lower prevalence. This will help determine if the neural network model that was developed in this study is generalizable to other patient populations. Potentially, a neural network could be developed for children with OSA, as PSG is more difficult to perform in this specific population.

**CONCLUSION**

This study has shown that an optimally trained GRNN can accurately rule out OSA in a referral setting where the prevalence of OSA is high (i.e., 69%). Also, the neural network did not miss important cases of OSA. This neural network was developed from readily available clinical data found in most patient charts. Approximately 32% of all PSG studies could have been avoided by using this classification tool. Training with increased numbers of subjects can be anticipated to only improve network predictive performance. Prospective validation of this new prediction methodology is warranted. The limited capital costs and expenses associated with operating such an instrument suggest that significant savings may be realized by using this novel approach.

**REFERENCES**