1. ABSTRACT

Observational study evaluating the diagnostic efficacy and clinical utility of the new version of interpretation algorithm for Tester BRASTER thermography in the diagnosis of breast pathology in women.

keywords: breast cancer, liquid crystal contact thermography, Tester BRASTERTM

BRA/11/2014 was a prospective, multicentre, open-label, observational, non-interventional study, conducted in specialist breast diagnostic outpatient clinics in Poland by persons trained in the thermography procedure, under the supervision of specialist physicians. Contact thermography using the Tester BRASTER device was performed in 274 women who consented to participate in the study and disclose the medical records. Out of this group, the final analysis included: 95 women aged 25–49 years with prior breast ultrasound scan assessed as BIRADS-US 4 or 5 (group A), 73 women aged ≥ 25 years with prior breast ultrasound scan assessed as BIRADS-US 1 or 2 (group B), and 87 women aged ≥ 50 years with prior breast ultrasound scan assessed as BIRADS-US 4 or 5 (group C). In total, the analysis included the testing results obtained in 255 women.

The primary objective of the study was to evaluate the diagnostic efficacy of the new versions of the interpretation algorithm for thermographic images obtained by liquid crystal contact thermography (TA-02 and TA-03), and to compare them with the previous version (TA-01).

The secondary objectives of the study were: 1) to verify the usefulness of liquid crystal matrix with a wide range of thermal detection (31°C–37°C), so-called yellow matrix ("IV"); 2) to compare each version of algorithm interpretation and classification of the result of breast thermography (TA-01, TA-02, TA-03) obtained using the Tester BRASTER device with the results obtained in the BRA/03/2013 study (THERMACRAC); 3) to validate the Automatic Interpretation System; and 4) to assess the safety of device use in clinical practice. The usefulness verification was done on the basis of clinical material in the form of thermographic data recorded with the Tester BRASTER device, and data from imaging and histopathology

examinations obtained in the process of standard diagnosis and differentiation of breast cancer in women.

For statistical purposes, the interpretation of thermographic testing was conducted according to the algorithms developed by BRASTER S.A. on the basis of past experience, based on a holistic method of determining thermal asymmetry and classification of the recorded hyperthermic changes. The interpretation was done by an independent radiological team of three persons, who had limited access to the patients' clinical data.

Additionally, the Automatic Interpretation System has been validated – it is a computer expert system developed on the basis of a set of rules relating to thermal and structural asymmetry of the breast.

The primary objective of the study, which was to compare the diagnostic efficacy of each developed algorithm for the interpretation of thermographic images, has been achieved. In the group of women < 50 years of age with an abnormal result of breast ultrasound scan (BIRADS-US 4 and 5), the sensitivity of thermography using the TA-01 algorithm was 66.7% (95% CI: 47.9; 82.0) at a specificity of 69.1% (95% CI: 57.4; 79.1). Statistics C was 0.679 (95% CI: 0.573; 0.785). The same parameters evaluated by the modified TA-03 algorithm were: sensitivity 81.5% (95% CI: 64.1; 92.6), specificity 87% (95% CI: 79.7; 92.4). Statistics C was 0.842 (95% CI: 0.761; 0.924). When comparing the predictive values in this group for each assessment algorithm, it was shown that the positive predictive value increased from 46.1% (95% CI: 31.2; 61.6) for the TA-01 algorithm to 71.0% (95% CI: 53.7; 85.8) for the TA-03, and the respective negative predictive value increased from 85.4% (95% CI: 74.4; 92.9) to 92.2% (95% CI: 83.7; 97.0). A comparison of the TA-01 and TA-03 (modified) algorithms in this group for statistics C reached significance in favour of the latter algorithm, modified TA-03 (p=0.0002). Similarly, in the group of women > 50 years of age with an abnormal result of breast ultrasound scan (BIRADS-US 4 and 5), the sensitivity of thermography using the TA-01 algorithm was 75% (95% CI: 64.1; 83.9) at a specificity of 60% (95% CI: 35.3; 81.3). Statistics C was 0.675 (95% CI: 0.537; 0.813). The same parameters evaluated by the modified TA-03 algorithm were: sensitivity 77.8% (95% CI: 67.2; 86.2), specificity 62.5% (95% CI: 48.5; 75.1). Statistics C was 0.701 (95% CI: 0.617; 0.786). In the group of women without breast pathology, the rate of false-positive

thermography was very similar to that observed in women with abnormal breast ultrasound without breast cancer (22.5% and 37.5% in women < 50 and ≥ 50 years of age, respectively). The obtained results cannot be directly compared to the results of the BRA/03/2013 (THERMACRAC) study due to the differences in obtaining and interpreting the thermographic images; however, the sensitivity and specificity obtained with the modified TA-03 algorithm in women < 50 years of age are significantly better.

The results of this study demonstrate good diagnostic efficacy of contact thermography in breast cancer detection and differentiation between malignant and benign pathologies of the breast in women < 50 years of age. It should be emphasised that the observed lower efficacy in women ≥ 50 years of age may be at least partially explained by the inclusion of women with breast ultrasound results in the category BIRADS US 5, where the likelihood of cancer is > 95%, in this age group. This could lead to an increase in the proportion of false negative results. The results indicate a very interesting direction in the application of the thermography technology for younger women, for whom the breast cancer prevention offer is fairly limited.

The results of validation of the automatic interpretation system for thermographic images have shown sensitivity of the validated test at the level of 75%, and a specificity of 76.1%, while the area under the ROC curve can be estimated at 75.6%. The results of validation showed a significant effect of the quality of the test procedure itself. The elimination of factors affecting the quality of testing would undoubtedly improve the efficacy of the system.

Principal Investigator:

Paweł Basta, MD, PhD
Coordinating Investigator
1st Chair of General Surgery, University Hospital in Krakow
ul. Kopernika 40, 31-501 Krakow

Sponsor:

BRASTER S.A.

Szeligi, ul. Cichy Ogród 7,
05- 850 Ożarów Mazowiecki