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# Formal analysis of the surgical pathway and development of a new software tool to assist surgeons in the decision making in primary breast surgery

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ABSTRACT

*Background:* The increased complexity of the decisional process in breast cancer surgery is well documented. With this study we aimed to create a software tool able to assist patients and surgeons in taking proper decisions.
*Methodology:* We hypothesized that the endpoints of breast cancer surgery could be addressed combining a set of decisional drivers. We created a decision support system software tool (DSS) and an interactive decision tree. A formal analysis estimated the information gain derived from each feature in the process. We tested the DSS on 52 patients and we analyzed the concordance of decisions obtained by different users and between the DSS suggestions and the actual surgery. We also tested the ability of the system to prevent post breast conservation deformities.
*Results:* The information gain revealed that patients preferences are the root of our decision tree. An observed concordance respectively of 0.98 and 0.88 was reported when the DSS was used twice by an expert operator or by a newly trained operator vs. an expert one. The observed concordance between the DSS suggestion and the actual decision was 0.69. A significantly higher incidence of post breast conservation defects was reported among patients who did not follow the DSS decision (Type III of Fitoussi, N = 4; 33.3%, p = 0.004).
*Conclusion:* The DSS decisions can be reproduced by operators with different experience. The concordance between suggestions and actual decision is quite low, however the DSS is able to prevent post-breast conservation deformities.



## Introduction

Prior to the historical trials on breast conservation, a mastectomy was the only surgical choice for primary treatment of breast cancer. Once the safety of glandular preservation had been established at the beginning of the 1980s, a second possible treatment could be offered to patients [1–6].

Initially, partial mastectomies appeared to guarantee integrity, but quite soon it became clear that breast conservation in some cases may not yield satisfying results [7,8].

Sometimes the cosmetic appearance after these operations was rather poor with visible scarring and severe deformities of the mammary shape. Several studies confirmed unsatisfactory results, even for breast-conserving surgery, in up to 20% of cases [9,10].

These failures initiated some reports regarding techniques derived from cosmetic surgery (breast reductions, mastopexies) to remove breast tumors without deformities [11–13].

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The advent of primary systemic therapies has also increased the number of possible therapeutic choices in the hands of surgeons [14,15].

Post-mastectomy radiation therapy (PMRT), which has recently shown increased indications, may also interfere with the pathway of breast reconstruction [18–23].

This information regarding the possible failures of breast conservation and good outcomes of mastectomy and reconstruction, coupled with an increase in patients' awareness, has generated a very complex and multifactorial decisional pathway [24–33].

With this study, we aimed at creating a prototype software tool capable of assisting patients and surgeons in making proper decisions. We tested it in a short cohort of patients in order to provide a preliminary validation of this instrument. We assessed the reproducibility and repeatability of the clinical procedure, the actual applicability of the proposed decisions, and the effects on postoperative residual defects.

## Methods

### *Endpoints, decisional drivers, creation of subcategories of disease*

In order to analyze the decision process, we created a set of possible endpoints of the surgical treatment of breast cancer. These were identified as safe removal of breast cancers on negative margins, avoiding disfiguring cosmetic results, and preserving good quality of life, thus putting the patient at the center of the decision process.

We hypothesized that these endpoints could be addressed by combining a set of decisional drivers that include morphological elements (breast shape and size) and topographic aspects related to cancer location, size, and stage in association with patients' preferences regarding surgical techniques as described in Table 1. We created four subcategories for volume according to bra size. Breast ptosis was classified into three subgroups using a modification of the classification of Regnault [23]. We also included in the "moderate ptosis" group patients with pseudo-ptosis and glandular ptosis to reduce the number of possible combinations. The breast was subdivided into seven subunits to locate the lump. Cases for which a mastectomy was the only possible choice did not include the assessment of tumor size, location, and risk of positive margins.

For patients affected by early-stage invasive cancer that can be treated with breast-preserving surgery, we decided to convey also the information on the risk of positive margins derived from a validated software tool named *breastconservation!* [17]. However, a high risk of positive margins was not per se an indication to perform wider excisions or mastectomies. The use of this tool was valid only for patients with invasive cancer.

Patients' preferences were investigated by doctors and breast care nurses during pre-op sessions using specific leaflets and multimedia tools [34]. We subcategorized patients' wishes according to three subcategories: "minimal aggressiveness," "maximum reshape," and "mastectomy."

At the end of this process, we identified four subgroups named as "ESBC" (localized invasive cancers with or without a minor ductal carcinoma in situ (DCIS) component), "DCIS localized" (small DCIS suitable for breast conservation), "MULTICENTRIC" (early-stage disease widespread in the breast, including DCIS), and "LABC" (locally advanced cancers requiring multimodality treatment, including radiation).

The decisional elements were combined manually in an electronic spreadsheet; each combination was considered as a single clinical case and associated with the most suitable surgical option by a panel of experienced oncoplastic surgeons. The final surgical suggestion was established according to current standard practice and previous observation reported by the senior authors of the paper [21,27,35–40].

### *Formal analysis and design of the decision tree*

The decisional process was analyzed according to the Iterative Dichotomiser 3 (ID3) algorithm. This allowed the creation of a navigable decision tree and a prototype decision-support system software (DSS) tool [41]. The information gain IG (A,S) measures how much uncertainty in S was reduced after splitting set S on an attribute A. It was calculated taking into consideration the subtraction between the information entropy of a specific subset of records and the sum of the entropies related to each value of one single attribute. Using this method, we choose iteratively the attribute that minimizes the amount of entropy of a specific subset of records as a node of the decision tree. In each subgroup, the highest value identifies the decisional driver providing the highest amount of information to the decisional pathway.

### *Preliminary clinical testing*

Once the DSS was available, we tested it on 52 patients to verify its clinical usability in a single unit in Catania-Ospedale Cannizzaro from November 2013. Patients affected by non-metastatic disease and candidates of any kind of surgical treatment (excluding secondary procedures, delayed reconstructions, surgery for local control in patients with disseminated disease) were admitted to this study. Current standard guidelines for treatment of breast cancer in our unit were strictly followed for either surgery and radiotherapy or other adjuvant treatments. All patients involved in this study signed a proper informed consent.

First of all, we investigated the repeatability of the suggestion produced by the DSS. We verified the concordance between the decision produced by an expert operator at two different times (during the last consultation and the night before the operation). Afterwards, we compared the output obtained by a newly trained surgeon with that of an expert one. Finally, we assessed the number

**Table 1**
List of decisional drivers.

| T-Stage or Multicentric disease | Location[a] | Volume | Ptosis | Risk of positive margins[b] | Pt wishes |
|---|---|---|---|---|---|
| T > 2 cm | Central | Minimal | Nil | High | Mastectomy |
| T < 2 cm | Upper | Medium | Moderate | Intermediate | Max. reshape |
| LABC | Lower | Large | Severe | Low | Min. Aggressiveness |
| DCIS<4 cm | Upper outer | Very Large | | | |
| Multicentric Invasive/Extensive DCIS | Upper inner | | | | |
| | Lower outer | | | | |
| | Lower inner | | | | |

[a] Not assessed for LABC Multicentric/extensive DCIS.
[b] Not assessed for LABC Multicentric/extensive DCIS and localized DCIS.

of times the actual surgical decision was concordant to that suggested by the DSS (last consultation).

As a secondary endpoint, we estimated the ability of the DSS to prevent post-breast-conserving therapy defects. Patients treated by breast-conserving surgery were observed postoperatively at 3 months, every 3 months during the first year, and then every 6 months by two surgeons (GC, VU) for the evaluation of residual deformities using the scale proposed by Fitoussi et al. [41]. The score of patients who followed the DSS suggestions was compared with that of those who refused the proposal of the software tool.

The medium follow-up was 21.6 months (range 16.4–27.1). Finally, to assess the length of the process the median number of consultations required to reach a decision using the DSS was also calculated.

### *Statistical analysis*

Continuous variables were expressed as mean and standard deviation and categorical variables as absolute number and percentage. Differences in characteristics of patients between groups were tested by exact Pearson chi-squared test for continuous and categorical variables. Exact binomial confidence intervals were calculated for proportions. All statistical tests were two-sided and $p$-values<0.05 were regarded significant. The data were analyzed using SAS version 9.2 (SAS Inc., Cary, NC, USA).

## Results

We developed a prototype software tool to assist surgeons in making decisions in oncoplastic surgery of the breast (DSS, Figs. 1–2). We generated a total of 2592 combinations subdivided, respectively, into 2268 for the group “ESBC,” 252 for the “localized DCIS” group, 36 for the “MULTICENTRIC” group, and 36 for the “LABC” group. In the group “ESBC,” the operator could also input data regarding the risk of positive margins. The total number of final suggestions was 97 (Fig. 3). The decision trees obtained are visible in the Supplementary Material in Figs. 4–7. A navigable version was also produced (demo visible at link: http://www.francescopappalardo.net/oncoplastic_decision_tree). The estimate of the information gain (GAIN) calculated on the four databases demonstrated that patients' wishes are the root of the decisional tree in all the subgroups we created (Table 2). The highest value is always associated with patients' wishes (GAIN = 1.18 for ESBC, 1.09 for localized DCIS, 1.00 for Ext DCIS, 1.29 for LABC).

The baseline characteristics of the population are described in Table 3.

Patients wanting a minimally aggressive surgical approach were 59.6%. A smaller proportion of the sample (19.2%) belonged to the group whose surgical preference was indicated as “mastectomy.” A median of three sessions was necessary to reach a surgical decision using the DSS.

The retesting by the same expert operator showed an observed concordance (OC) of 0.98 (0.90–0.99, 95% CI), and in the comparison between the first test by an expert operator and the test performed by a second surgeon, the OC value was 0.88 (0.77–0.96, 95% CI). The OC between the actual decision and the decision suggested by the DSS was estimated to be a value of 0.69 (95% CI, 0.55–0.81). The suggested decision was not followed by a correspondent actual decision in a total of 14 cases (Table 4).

We performed 20 (38.4%) wide local excisions (with or without any kind of nipple areola complex repositioning), 13 (25%) therapeutic mammoplasties (of which eight were unilateral), 14 (26.9%) skin- or nipple-sparing mastectomy and immediate reconstruction, and two (3.8%) radical mastectomies. Three (5.7%) patients underwent neo-adjuvant chemotherapy before surgery.

The incidence of post-breast-conservation residual defects was investigated in this series. Twenty-nine patients (87.7%) were reported as type I and II in the classification of Fitoussi. Four patients (12.1%) were classified as type III (Table 5). We found that all patients with severe deformities (type III) belonged to the “no-

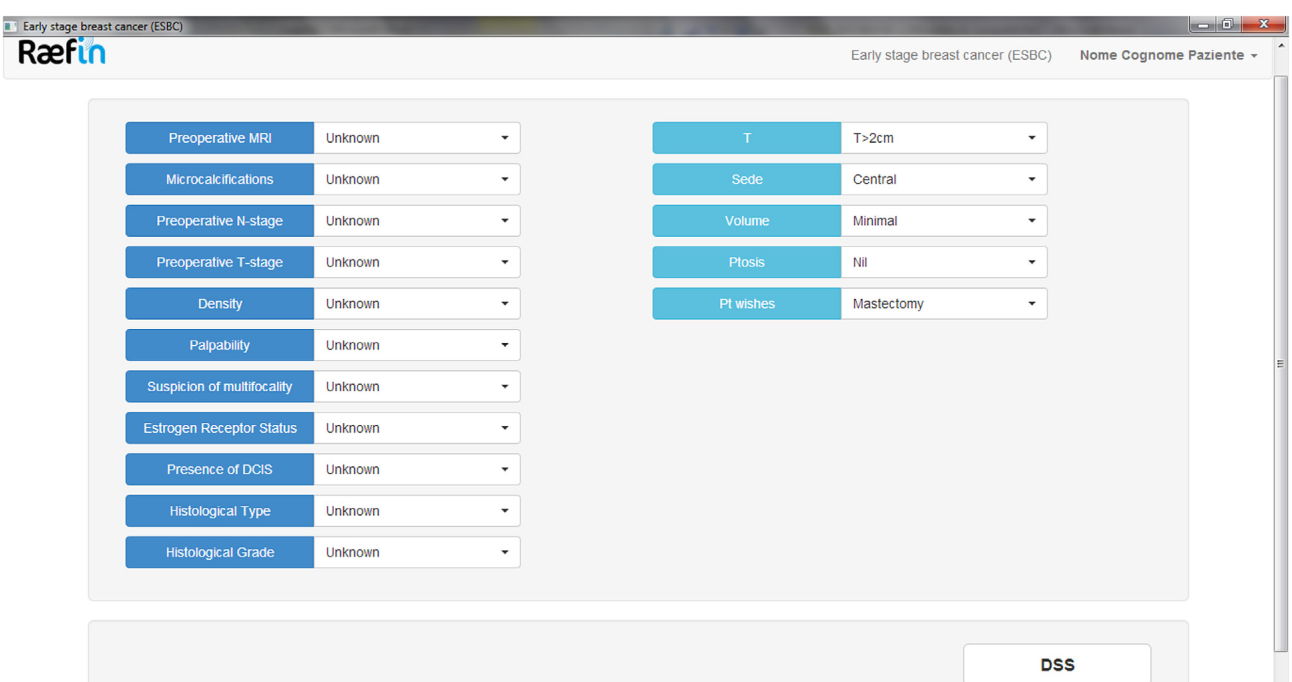


**Fig. 1.** Prototype interface of the CDSS.

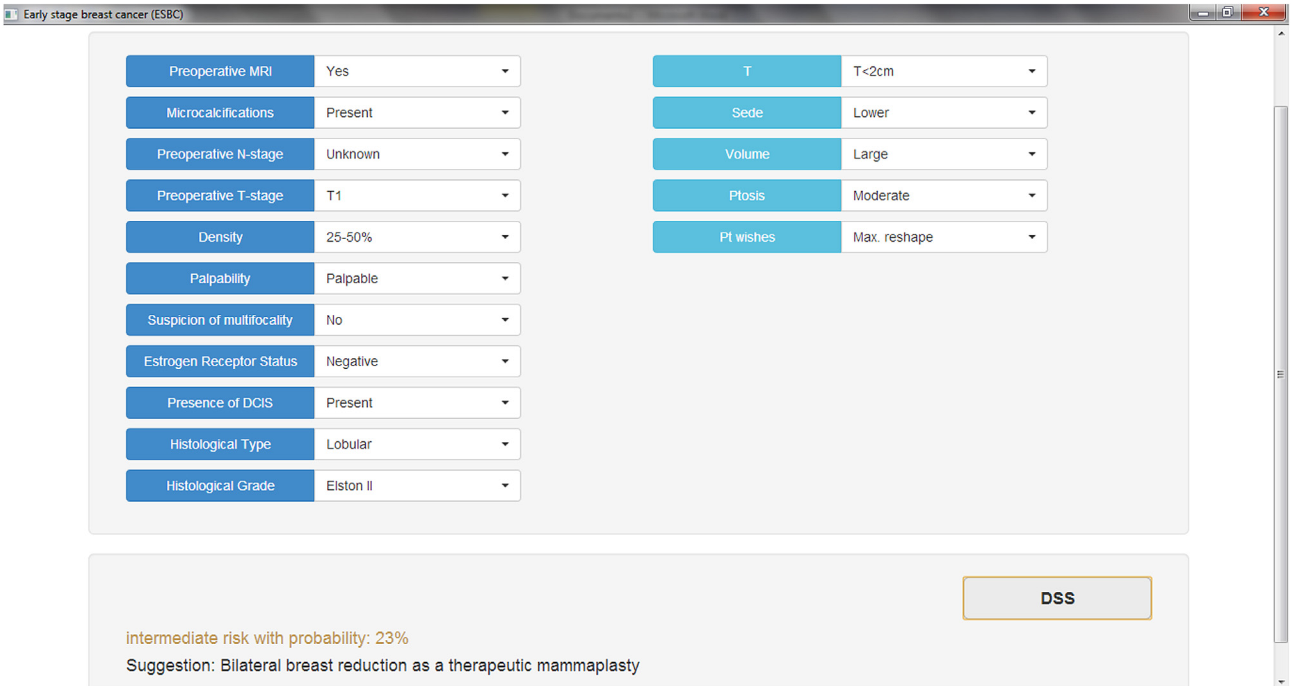


**Fig. 2.** Prototype interface of the CDSS with suggested decision.

concordance" subgroup (four patients, 33.3% vs. 0, $p = 0.004$) (Table 6). Women who did not follow the suggestions of the DSS were older, with lumps located in the upper-inner quadrant, between the superior quadrants of the breast, or in the lower outer quadrant. They also had small or very large breasts more frequently (respectively, 25% vs. 0 and 16.6% vs. 9.5%, $p = 0.04$) and a lower risk of positive margins with breast conservation (91.6% vs. 57.1, $p = 0.04$) (Table 7).

All patients with type III defects were older than 75. Three patients (9.0%) who were advised to undergo a mastectomy by the DSS indicated their preference for breast-conserving surgery and retained an acceptable breast shape. Finally, eight (24.2%) patients who indicated a minimal aggressive approach were recommended to undergo a unilateral breast reduction, for which they refused to undergo a simpler wide local excision. Three of them reported a distortion of the final breast shape.

## Discussion

The increased complexity of the decisional process in breast cancer surgery is well documented [10,42–47].

Several studies have tried to overcome this condition, proposing algorithms, flow charts, and nomograms to support the final decision regarding surgical treatment [24,42,43,48–51].

In 2012, Clough et al. [42] proposed a quadrant-per-quadrant approach to oncoplastic techniques for breast cancer, which tailored the mammoplasty to each tumor location. A nomogram was proposed to select the correct technique according to each quadrant, but considerations regarding breast shape and size were not included. No suggestions were provided for tumors located in the central quadrant. This study followed a previous one by the same author. Even in this case, considerations on breast shape and volume were missing.

Munhoz et al. [50] proposed an algorithm based on the breast size in relation to tumor location and extension of resection. The authors tested it on 206 patients, claiming that complications were similar to those reported in other clinical series. Subjective or objective evaluation of final results was not assessed. The increased complexity produced by adding the volume estimates is clearly visible in the diagrams displayed, which are less readable compared with those proposed by Klough.

Kronowitz et al. [49] presented a management algorithm for repairing partial mastectomy defects based on some clinically relevant parameters, including timing of reconstruction in relation to radiation therapy, status of the tumor margin, extent of breast skin resection, breast size, and whether the cosmetic outcome would be better after a total mastectomy with immediate breast reconstruction. The study is not associated with any clinical validation and the flow chart presented is very complex. It is to be noted the authors used a formally correct graphic language.

In addition, other flow charts and diagrams have been used in recent times to assist decisions in the field of mastectomy and reconstruction, especially when PMRT is required [24,52].

Many other examples of flow charts, decision makings, and algorithms can be identified. Most of these lack validation and may be considered mere experts' opinions; the large majority of them are strictly oriented to specific clinical conditions (PMRT, oncoplastic surgery, etc.). None of them include a formal analysis of the process or the integration of patients' wishes in the decision process.

In this study, we tried to overcome most of the limitations of previous experiences. First of all, we extended our pathway to the largest possible combination of cases in order to get an omnicomprehensive view of the surgical treatment. We associated most of the decisional drivers proposed by older studies, including estimates of breast volume and ptosis, the location of the lesion, and the amount of tissue to be removed. It is to be noted we added to these elements an evaluation of patients' preferences regarding the surgical approach. To our knowledge, this is the first time that such an appraisal has been integrated

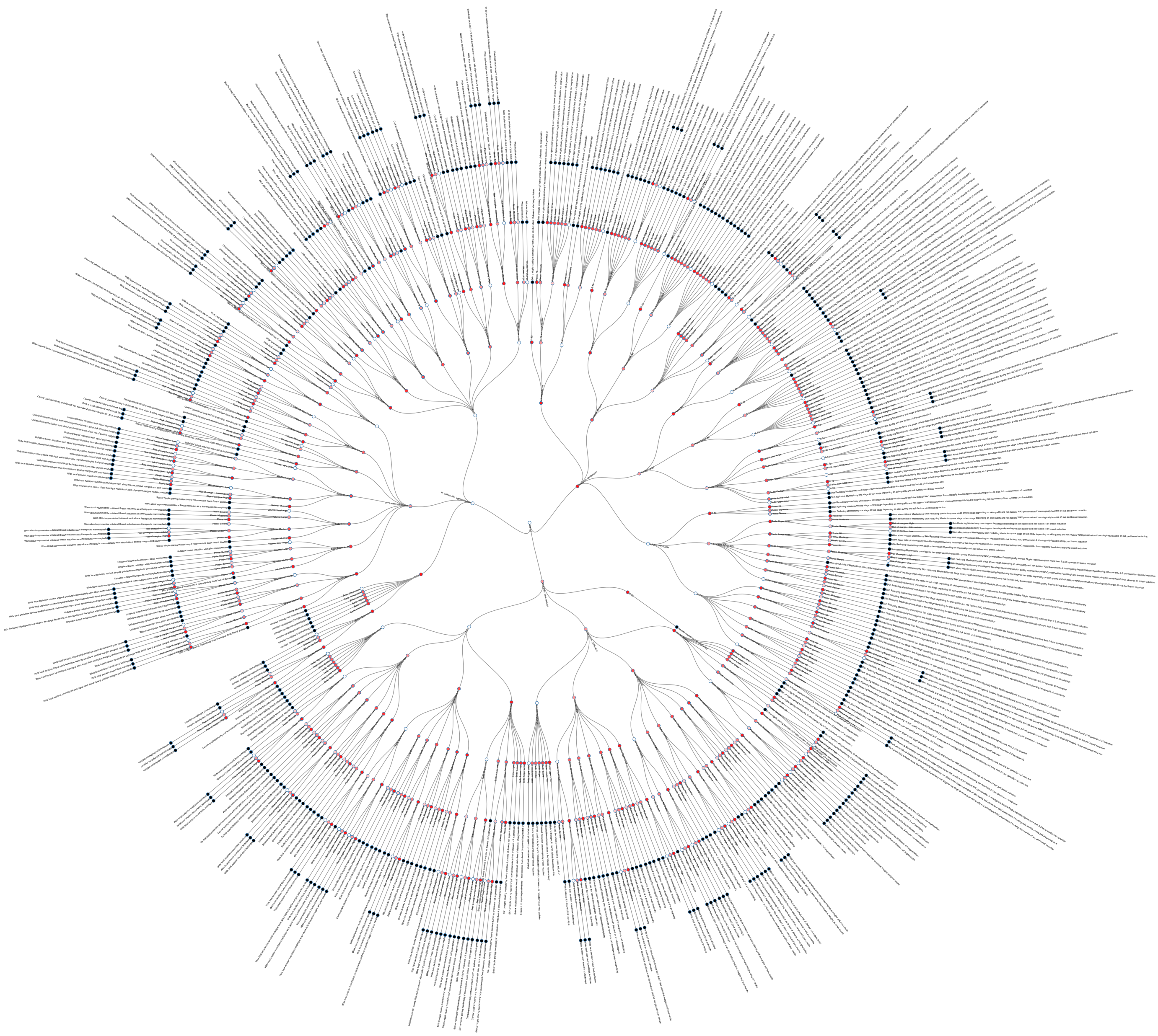

**Fig. 3.** Extended decision tree for ESBC ("the genome-like decision tree").

**Table 2**
Values of information gain according to each clinical subgroup.

| ESBC | | Localized DCIS | |
|---|---|---|---|
| T | GAIN = 0.85 | T | GAIN = 0.62 |
| Location | GAIN = 0.75 | Location | GAIN = 0.55 |
| Volume | GAIN = 0.99 | Volume | GAIN = 0.79 |
| Ptosis | GAIN = 0.36 | Ptosis | GAIN = 0.21 |
| Risk of margin+ | GAIN = 0.03 | **Pt wishes** | **GAIN = 1.09** |
| **Pt wishes** | **GAIN = 1.18** | | |
| **LABC** | | **Ext_DCIS** | |
| T | GAIN = 0.91 | T | GAIN = 0.91 |
| Volume | GAIN = 1.00 | Volume | GAIN = 0.89 |
| Ptosis | GAIN = 0.45 | Ptosis | GAIN = 0.23 |
| **Pt wishes** | **GAIN = 1.29** | **Pt wishes** | **GAIN = 1.00** |

into a surgical decisional pathway. The combination of all these elements created a very complex twist, poorly manageable in clinical practice. Thus, the main output of this study is the creation of a DSS tool in which all the drivers can be combined electronically to generate a surgical suggestion. Besides this system, we also created a navigable decision tree that allows surgeons with lesser experience to search among all the possible combinations to increase their knowledge. The design of the decision trees was also independently analyzed, confirming that we assigned the highest weightage to patients' preferences. The intricacy of the whole system is visible in Figs. 4–7 and it resembles the graphic style of a genome.

We used this system on a small cohort of randomly assigned patients who underwent surgery by a single oncoplastic surgeon. The median number of consultations was quite high, and we may suppose that it could be even higher as some of the patients had

**Table 3**
Distribution of decisional drivers among population.

| T-Stage or Multicentric disease | N = 52 | Location[a] | N = 42 | Volume | N = 52 | Ptosis | N = 52 | Risk of margin+[b] | N = 40 | Pt wishes | N = 52 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| T > 2 cm | 3 (5.8) | Central | 3 | Minimal | 10 (19.2) | Nil | 14 (26.9) | High | 25 (48.1) | Mastectomy | 10 (19.2) |
| T < 2 cm | 37 (71.2) | Upper | 14 (26.9) | Medium | 16 (30.8) | Moderate | 18 (34.6) | Intermediate | 6 (11.5) | Max. reshape | 11 (21.2) |
| LABC | 2 (3.8) | Lower | 4 (7.7) | Large | 21 (40.4) | Severe | 20 (38.5) | Low | 8 (15.4) | Min. Aggressiveness | 31 (59.6) |
| DCIS<4 cm | 2 (3.8) | Upper outer | 9 (15.4) | Very Large | 5 (9.6) | | | | | | |
| MULTICENTRIC Invasive/Extensive DCIS | 8 (15.4) | Upper inner | 6 (11.5) | | | | | | | | |
| | | Lower outer | 5 (9.6) | | | | | | | | |
| | | Lower inner | 1 (1.9) | | | | | | | | |

[a] Not assessed for LABC Multicentric/extensive DCIS.
[b] Not assessed for LABC Multicentric/extensive DCIS and localized DCIS.

**Table 4**
Concordance analysis.

| Comparison | Observed concordance (95% CI) |
|---|---|
| Expert user (Assessment 1) vs. Expert user (Assessment 2) | 0.98 (0.90–1.00) |
| Expert user (Assessment 1) vs. Non-expert User A | 0.88 (0.77–0.96) |
| Expert user (Assessment 1) vs. Actual Decision | 0.69 (0.55–0.81) |

**Table 5**
Incidence of post-breast-conservation defects according to Fitoussi.

| | N (%) |
|---|---|
| Type I/II | 29 (87.7) |
| Type III | 4 (12.1) |

**Table 6**
Incidence of post-breast-conservation defects in patients whose actual surgery is concordant versus not concordant with DSS suggestions.

| | Concordance (N = 21)% | No concordance (N = 12)% | P-value |
|---|---|---|---|
| Fitoussi Score | | | 0.004 |
| Grade I | 19 (90.4) | 5 (41.6) | |
| Grade II | 2 (9.5) | 3 (25.0) | |
| Grade III | 0 | 4 (33.3) | |

**Table 7**
Incidence of decisional drivers among patients who followed the DSS suggestion (concordance) and those who did not (no concordance).

| | Concordance (N = 21) | No concordance (N = 12) | P-value |
|---|---|---|---|
| **Age years**, mean (SD) | 64.58 (15.8) | 51.1 (13.0) | **0.004** |
| **Extent of disease** | | | 0.206 |
| Localized DCIS | 3 (14.2) | 0 | |
| T < 2 cm | 18 (85.7) | 12 (100%) | |
| T > 2 cm | 0 | | |
| **Breast Location** | | | **0.009** |
| Central | 1 (4.7) | 0 | |
| Upper Outer | 8 (38.0) | 0 | |
| Upper Inner | 0 | 3 (25.0) | |
| Upper | 7 (33.3) | 5 (41.6) | |
| Lower outer | 1 (4.7) | 4 (28.5) | |
| Lower inner | 1 (4.7) | 0 | |
| Lower | 3 (14.2) | 0 | |
| **Breast Volume** | | | **0.04** |
| Small | 0 | 3 (25) | |
| Medium | 8 (38.0) | 1 (8.3) | |
| Large | 11 (52.3) | 6 (50.0) | |
| Very large | 2 (9.5) | 2 (16.6) | |
| **Ptosis** | | | 0.2 |
| No ptosis | 2 (9.52) | 1 (8.33) | |
| Moderate | 11 (52.3) | 9 (75.0) | |
| Severe | 8 (38.0) | 2 (16.6) | |
| **Risk of positive margins** | | | **0.044** |
| Low | 12 (57.1) | 11 (91.6) | |
| Intermediate | 3 (14.2) | 1 (8.3) | |
| High | 3 (14.2) | 0 | |
| N/A | 3 (14.2) | 0 | |
| **Patient's wishes** | | | 0.18 |
| Mastectomy | 0 | 0 | |
| Max reshaping | 5 (23.8) | 0 | |
| Min aggressiveness | 16 (76.1) | 12 (100) | |

already had a positive imaging and core biopsy at the time of the first consultation. Certainly, the central role of the patient and the increased awareness of the process had an impact on this. However, the centered approach of the patients demonstrated its non-negligible role in improving the outcome of the oncological treatment several times [28,53–55].

With this test, we investigated the repeatability of the procedure in the hands of an expert operator and in that of a second newly trained surgeon. We confirmed a good concordance both when the DSS is used by an expert in two different sessions and when the output of the experienced operator is compared with that of the newly trained one.

To better understand the value of the DSS, we also assessed the concordance between the actual surgical decision and that suggested by the system. Not surprisingly, this value was quite low. Specifically, we noted that four patient candidates of the DSS for some kind of minimal breast reshape refused it and underwent a standard wide local excision. This of course generated a distortion in the postoperative appearance of their breast (classified as grade III according to Fitoussi). Interestingly, all these patients were older than 75 and had associated comorbidities. This trend may indicate the need for adding other drivers to the DSS (such as age and comorbidities) and a fourth subcategory of patients wishing an ultra-minimal surgical approach. Among the patients who refused the suggestion of the DSS, we also had three cases who were advised to undergo a nipple-sparing mastectomy and reconstruction for a poor breast to tumor ratio. They preferred to undergo a wide local excision, and despite the difficult position of the cancer, the final results did not produce any major deformity. We believe that the suggestion to undergo a mastectomy is due to the original conception of our framework, which predated the publication of convincing evidences regarding the usefulness of leaving wide resection margins after breast conservation for invasive cancers [56,57].

In view of these findings and by the time we gain more experience, we will consider any revision in the framework.

We acknowledge that this work may have several limitations. First of all, the whole pathway is based on the collation of standard clinical practices and previously reported experiences of the senior authors. Despite the high level of evidence presented by each single study supporting the framework, this is not the result of a comprehensive systematic review. Therefore, the final level of evidence provided is still very low and can be considered more or less like an expert opinion. To increase the power of the study and to get a final validation, we are planning to proceed in two phases. A learning phase will allow the collection of prospective information on the outcome of patients, which may or may not follow the indication of the DSS. This will be used to tailor the DSS to always provide the suggestion associated with the best outcome. Once this phase is completed, we will test the tool on a randomized population to get the final validation with the highest level of evidence.

## Conflict of interest statement

None declared.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.breast.2016.06.004.

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