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# STATISTICAL ANALYSIS PLAN

Version 1.0, dated 26-Nov-2024

Study: CS-BCL-EU2021  
NCT06461663


SPONSOR: CairnSurgical Inc.

## **An Interventional, Post-Market Study to Evaluate the Performance of a Custom-made Medical Device, “Breast Cancer Locator Guidance (BCL)” System, in Breast-conserving Surgery (BCS)**

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Statistical Analysis Plan is based on the 1MED global template (Version 2.0) for clinical studies. Template version: Working 1.0

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## Document History

| Version | Date        | Authors            | Description |
|---------|-------------|--------------------|-------------|
| 0.1     | 26-Nov-2024 | Valeria Valsassina | Version 0.1 |
|         |             |                    |             |
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### Signature page

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## List of Abbreviations and acronyms

|             |                             |
|-------------|-----------------------------|
| <b>AE</b>   | Adverse Event               |
| <b>BC</b>   | Breast Cancer               |
| <b>BCL</b>  | Breast Cancer Locator       |
| <b>BCS</b>  | Breast Conserving Surgery   |
| <b>BMI</b>  | Body Mass Index             |
| <b>BP</b>   | Blood Pressure              |
| <b>CI</b>   | Confidence Interval         |
| <b>CIP</b>  | Clinical Investigation Plan |
| <b>CRF</b>  | Case Report Form            |
| <b>DBL</b>  | Database Lock               |
| <b>DCIS</b> | Ductal Carcinoma In Situ    |
| <b>eCRF</b> | Electronic Case Report Form |
| <b>EOS</b>  | End Of Study                |
| <b>FAS</b>  | Full Analysis Set           |
| <b>HR</b>   | Heart Rate                  |
| <b>IBC</b>  | Invasive Breast Cancer      |
| <b>ICF</b>  | Informed Consent Form       |
| <b>IFU</b>  | Instruction For Use         |
| <b>IP</b>   | Investigational Product     |
| <b>MRI</b>  | Magnetic Resonance Imaging  |
| <b>PMR</b>  | Positive Margin Rate        |
| <b>PPS</b>  | Per Protocol Set            |
| <b>SAE</b>  | Serious Adverse Event       |
| <b>SAP</b>  | Statistical Analysis Plan   |
| <b>SAS</b>  | Safety Analysis Set         |
| <b>TLF</b>  | Tables Listings and Figures |
| <b>WDM</b>  | Water Displacement Method   |

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## 1. Study documents, design, objective, and database coding

### 1.1. Introduction

This Statistical Analysis Plan (SAP) is based on the relevant sections of the study protocols CS-BCL-EU2021\_CIP\_V2.0\_21.11.2023\_ITA CH and CS-BCL-EU2021\_CIP\_V2.0\_SubAmend 2\_GERMANY, Version 2.0, released on 21 November 2023.

The current Statistical Analysis Plan (SAP) includes detailed procedures for executing the statistical analysis of the primary and secondary variables and other data.

All analysis data sets, and statistical output will be produced by the statistics department at Via Campagna 13, Agno (CH) of 1MED SA using SAS software [1] current version .

### 1.2. Overall Study Design

This is an interventional, post-market, multicentre clinical investigation aimed to enrol patients who require the tumor to be localized in order for the surgeon to perform BCS. The study will include enrollment at 6 centers in Europe. The countries involved are Germany, Italy, Switzerland. The investigation will be useful to collect Investigational Product (IP) performance/safety evidence in Europe.

Each Subject, after signing the Informed Consent Form (ICF), will enter into a screening phase (V0) during which several assessments (e.g., demographics, medical history, blood sample collection, evaluation of available prone MRI and core biopsy pathological results) will be conducted. At visit 1 (V1), the Subject will undergo supine MRI (10-40 days before surgery), from which the 3D breast image and BCL will be made. At visit 2 (V2) the patient will undergo BCS using the BCL System. Soon after surgery and prior discharge, potential AEs will be assessed. On the same day, the

specimen volume will be determined, and the specimen mammogram will be performed. The excised specimen will be sent to the Pathology lab for analysis. The results of the positive margin rate (PMR) will be obtained within 14 days.


At visit 3 (V3), follow-up assessments (including physical examination, and AEs review) will be performed. At the end of study (EOS/V4), AEs will be assessed, and patients will be asked to express their satisfaction with the BREAST-Q. All study procedures are schematized in the flowchart (section 1.2.5).

#### 1.2.1. Randomization

Considering the design of the study, a randomization procedure is not required.

#### 1.2.2. Treatment

The BCL System is a patient-matched Breast Conserving Surgery (BCS) guidance device derived from

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supine breast magnetic resonance imaging (MRI) data. The device allows the surgeon to transfer surgical cues associated with a patient's breast and breast cancer to help guide the surgeon with the tumor resection procedure. An optional web-based interactive surgical plan Visualizer will be provided, displaying a 3D model of the BCL, tumor, and chest wall with markers indicating the closest points and distances between the tumor, skin, and chest wall/muscle.

The procedure consists of three main steps as described in the BCL System IFU:

- Step 1. Pre-surgical imaging and image transfer;
- Step 2: breast tissue marking using the BCL;
- Step 3: surgery and tumor removal.

At visit 2 (V2), all the enrolled patients meeting all the inclusion and none of the exclusion criteria were treated BCS using the BCL System.

### 1.2.3. Sample Size


The positive margin rate (PMR) with the use of BCL is expected to be < 5% based on a previous study [2]. Assuming a true PMR of 3% and applying the exact or Clopper-Pearson method for a single binomial proportion then a sample size of N=35 patients who have undergone surgery with the BCL and have had a margin assessment will achieve a confidence interval with total width of 15%. The upper limit of this confidence interval (18%) is lower than the currently observed positive margin rate using the standard of care.

An exact binomial confidence interval will be calculated using the actual PMR. The withdrawal of patients before the surgery with BCL will be considered as drop-out.

Statistical power calculation was performed using SAS® software [1], version 9.4.

### 1.2.4. Blinding

Considering the design of the study a blinding/unblinding procedure is not required.

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### 1.2.5. Flow Chart of the Study

The study visits and related procedures are summarized in the flowchart below.

| Determinations   | Screening & Enrollment (V0) <sup>A</sup> | Visit 1 (V1)<br>Supine MRI <sup>A</sup> | Visit 2 (V2)<br>Surgery           |                    | Visit 3 (V3)<br>Follow-Up     | Visit 4 (V4)<br>End Of Study (EOS) |
|--|--|---|-----------------------------------|--------------------|-------------------------------|------------------------------------|
|  | Within 15-30 days before V1              | Day 0 <sup>A</sup>                      | Within 10-40 days from supine MRI | Prior to discharge | 2 weeks ± 7 days post surgery | 6 weeks ± 7 days post surgery      |
| ICF <sup>A</sup>   | X  |   |                                   |                    |                               |                                    |
| Inclusion/Exclusion criteria   | X  |   |                                   |                    |                               |                                    |
| Medical history <sup>B</sup>   | X  |   |                                   |                    |                               |                                    |
| Demographic data (including age, smoking habits and alcohol use)         | X  |   |                                   |                    |                               |                                    |
| Vital signs (BP, HR, O <sub>2</sub> saturation)                          | X  | X                                       | X                                 | X                  | X                             |                                    |
| Physical examination <sup>C</sup>  | X  |   |                                   | X                  | X                             |                                    |
| Blood samples (laboratory parameters) <sup>D</sup>                       | X  |   |                                   |                    |                               |                                    |
| Urine pregnancy test to all women of childbearing potential <sup>E</sup> | X  |   |                                   |                    |                               |                                    |
| Radiological assessment <sup>F</sup>                                     | X  |   |                                   |                    |                               |                                    |
| Supine MRI   |  | X <sup>A</sup>                          |                                   |                    |                               |                                    |
| Prone MRI  | X <sup>A</sup>                           |   |                                   |                    |                               |                                    |
| Provide tumor specimen to pathological lab <sup>G</sup>                  |  |   | X                                 |                    |                               |                                    |
| BCS with BCL <sup>H</sup>  |  |   | X                                 |                    |                               |                                    |
| 5 Likert Scale (completed by PI) <sup>I</sup>                            |  |   | X                                 |                    |                               |                                    |
| BREAST-Q   |  |   |                                   |                    |                               | X                                  |
| Adverse events (AEs)   | X  | X                                       | X                                 | X                  | X                             | X                                  |
| Concomitant medications  | X  | X                                       | X                                 | X                  | X                             | X                                  |
| Device deficiencies/incidents monitoring                                 |  | X                                       | X                                 |                    |                               |                                    |

#### Notes:


<sup>A</sup> Informed Consent Form (ICF) signed and dated, before any trial procedure is performed. In order to provide the Investigator with an adequate time frame to organize and perform the clinical tests and assess the inclusion/exclusion criteria on the Subject, the screening phase was set up a maximum duration of 30 days (V0). During this screening phase the size of tumor should be verified. If the volume of tumor resulted lower than 5mm after the prone breast MRI performed in the screening phase, the withdrawal of the patient will be considered as a screening failure. After the ICF is signed, a supine MRI will be scheduled as soon as possible but according to local standard procedure.

Data collected by supine MRI (performed at V1):

- tumor maximum diameter (cm), tumor volume and ideal specimen volume (mm<sup>3</sup>).

Data collected by prone MRI (performed at V0):

- presence of satellite lesion(s) (Y/N) and maximal tumor diameter (mm).

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<sup>B</sup> Medical history includes patient-reported bra cup size and documentation of any contraindications to MRI (e.g., implanted electrical devices exist), history of adverse reactions to gadolinium, breastfeeding or pregnancy.

<sup>C</sup> Physical examination includes weight, height, distance from sternal notch to the nipple, the circumference around the breast and arms, calculation of BMI, and specific documentation that the breast cancer cannot be palpated.

<sup>D</sup> Laboratory Tests include:

- serum creatinine levels to calculate the glomerular filtration rate (GFR), acid uric for renal dysfunction;
- complete blood count;
- electrolytes (sodium, potassium, chloride, bicarbonate).

<sup>E</sup> For females of childbearing potential only, urine pregnancy test will be performed with dipsticks supplied by the Investigator. Results must be available before any procedure.


<sup>F</sup> All Subjects will have had a mammogram and prone MRI assessment prior to enrollment. If breast ultrasound images are obtained, they will be available to the study team. The results from pathologic analysis of diagnostic core biopsy specimens, including IBC vs. DCIS, will be documented. Results of imaging studies should be obtained within 3 months of study enrollment.

<sup>G</sup> After the tumor specimen is removed:

- the specimen volume will be determined by water displacement,
- a specimen mammogram will be obtained and then the specimen will be sent to the pathologist for evaluation of the positive margins.
- the presence of invasive cancer in core biopsy (Y/N), presence of DCIS in core biopsy (Y/N), presence of invasive cancer in lumpectomy specimen (Y/N), presence of DCIS in lumpectomy specimen (Y/N), subtype of invasive cancer (ductal vs lobular vs other), Maximal tumor diameter on pathology report of lumpectomy specimen (mm), shave biopsy done during surgery (Y/N, and if done how many) will be recorded.

<sup>H</sup> Surgery will be scheduled 10-40 days after the supine MRI. Subjects will have a pre-surgical contrast-enhanced supine MRI. MRI images will be transmitted to CairnSurgical where a study radiologist will outline the tumor edges on the supine MRI. These supine MRI images will be used to fabricate a BCL using 3D printing. The Investigator will perform the BCS using the BCL device. Specimen volumes will be determined by water displacement. Specimen mammograms will be obtained. Additional shave biopsies may be taken after the initial tumor resection at the discretion of the investigator. The specimen will be sent to Pathology.

<sup>I</sup> If, for any reason, the PI is not able to fill the 5-point Likert Scale soon after surgery, the procedure must be completed prior discharge of the patient.

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### 1.3. Study Objective(s)

#### 1.3.1. Primary Objective(s)

The primary objective is to evaluate the performance of the BCL in reducing the positive margin rate when the BCL system is used to guide a surgeon performing partial mastectomy.

#### 1.3.2. Secondary Objective(s)

The secondary objectives of the study are:

- To calculate the specimen volume after BCL guided partial mastectomy;
- To evaluate the surgeon's perception of ease of use of the BCL system;
- To evaluate the safety and tolerability of BCL;
- To evaluate the patient's satisfaction;
- To compare the ideal specimen volume to the actual specimen volume and tumor volume;
- To record important clinical data on the removed specimens.


#### 1.3.3. Other Objective(s)

Not applicable for this study.

## 2. Study documents

The following documents were used in the writing of the present SAP:


- Study protocols:
  - "CairnS\_BCL\_CIP\_V2.0\_Amend1\_ITA-SWISS\_21November2023.pdf";
  - "CS-BCL-EU2021\_CIP\_V2.0\_SubAmend 2\_GERMANY\_21Nov2023.pdf"
- pCRF:
  - "CS-BCL-EU2021\_pCRF\_V2.0\_3.12.2023.pdf";
- Likert ease of use for BCL:
  - "CS-BCL-EU2021\_Likert ease of use BCL\_V1\_ENG\_05Oct2021.pdf"
  - "CS-BCL-EU2021\_Likert facilita uso BCL\_V1\_ITA\_05Oct2021.pdf"
- Likert ease of use for Visualizer
  - "CS-BCL-EU2021\_Likert ease of use Visualizer\_V1\_ENG\_05Oct2021.pdf"
  - "CS-BCL-EU2021\_Likert facilità uso Visualizer\_V1\_ITA\_05Oct2021.pdf"
- BREAST-Q:
  - "BREAST-Q BCT V2.0 English - Sat. w Breasts.pdf"
  - "BREAST-Q BCT V2.0 Italian IT (L) - Sat. w Breasts.pdf"
  - "BREAST-Q BCT V2.0 German DE (L) Sat. w Breasts.pdf"

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### 3. Database coding

AEs will be coded using MedDRA® dictionary version 27.0 (Lowest Level Term (LLT), Preferred Term (PT), and System Organ Class (SOC)).

To describe prior and/or concomitant medications, medications will be coded with active ingredients reported in English.

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## 4. Analysis Sets and Subgroups

### 4.1. Analysis sets


The data sets defined for the study in accordance with the study protocol are outlined in the following table.

|                            |   |
|----------------------------|---|
| Safety Analysis Set (SAS): | The "Safety Set" will include All patients undergoing surgery with the BCL System.  |
| Full Analysis Set (FAS):   | The "Full Analysis Set" will include All patients undergoing surgery with the BCL System.   |
| Per-Protocol Set (PPS):    | The "Per-Protocol Set (PPS)" will include all the FAS patients who (a) met all inclusion/exclusion criteria liable to affect the performance assessment, (b) did not present serious deviations of the protocol that may affect efficacy. |

Definition of major protocol deviations and selection of subjects accordingly will be performed prior to Database Lock (DBL).

### 4.2. Subgroups

Not applicable for this study.

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## 5. General Definitions and Naming Conventions

To avoid ambiguity during the analysis, a few definitions and conventions for data handling are described here.

### 5.1. Treatment Group Names and Labels

Due to the single-arm nature of the stage, no treatment group definition or label is required.

### 5.2. General Methodology and Presentation of the Results

All collected data will be presented through listings and tables.

To ensure effective presentation of results, if deemed necessary, listings shall be divided into two or more distinct outputs. Each newly created listing will maintain the original table number, followed by a consecutive alphabetical letter, and the original title; additional specifications regarding the contents of the listing may be included after the listing title.

In tables, default summary statistics for quantitative variables will be:

- Mean, Standard Deviation (SD), number of missing observations (N), minimum and maximum values, if all continuous variables of a specific section (i.e., vital signs, blood evaluation, etc.) could be considered normal;
- Median, Range Q1 - Q3, number of missing observations (N), minimum and maximum values, if at least one continuous variable of a specific section (i.e., vital signs, blood evaluation, etc.) couldn't be considered normal.

For simplicity, the mockup tables in this SAP use the first case. However, the final study report will reflect the appropriate case based on the data distribution.


For qualitative variables, the counts (N) and percentage (%) of patients with non-missing data per category will be the default summary presentation, and, where appropriate and present, the number of missing values as a "Missing" category.

Percentages will be calculated using as the denominator the number of all patients in a specified population or treatment group, unless specified otherwise. The denominator will be specified in a footnote to the tables for clarification if necessary.

All listings will be produced with reference to the set of All patients.

### Statistical Output Layout:

All tables will be presented for overall treatment group and all listings will be presented by patient ID, study visits and, if necessary, by study centers;


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The format for presentation of time variables will be hh:mm. The format for presentation of date variables will be dd/mmm/yyyy. Missing portions of dates will be represented on patients listings as dashed:

|                      |              |
|----------------------|--------------|
| <b>Complete date</b> | 15/Jan/2022  |
| <b>Unknown day</b>   | UNK/Jan/2022 |
| <b>Unknown month</b> | UNK/UNK/2022 |

Dates that are missing because they are not applicable for the patient will be presented as "UNK/UNK/UNK", unless otherwise specified.

Listings will be sorted by patient screening number unless specified otherwise.

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### 5.3. Visit Names and Labels

The names to be used in the analysis datasets and the labels to be used in the tables, listings and figures for the different study visits are defined below.

| Visit number | Visit name                | Visit label,<br>which appear in TLFs | Visit ID |
|--------------|---------------------------|--------------------------------------|----------|
| 01           | Screening & Enrollment V0 | Screening V0                         | V0       |
| 02           | Visit 1                   | V1                                   | V1       |
| 03           | Visit 2 Surgery           | Surgery V2                           | V2       |
| 04           | Visit 3 Follow-up         | Follow up V3                         | V3       |
| 05           | Visit 4 EOS               | EOS V4                               | V4       |


### 5.4. Visit Windows

In the study, 5 study visits were planned.

- The screening/baseline visit will be performed within 30 days before V1
- V1 will be performed at day 0
- V2 will be performed within 10/40 days from V1
- V3 will be performed at week 2  $\pm$  7 days from V2
- EOS visit will be performed after 6 weeks since V2  $\pm$  7 days.

### 5.5. Multiple testing

Not applicable for this study.

|  |                           |                  |                |
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## 6. Statistical Analysis: Definitions, Derivations, Calculations and Methodology

### 6.1. Baseline Characteristics

#### 6.1.1. Disposition of Patients

##### Collected Variables:

- Was Informed Consent signed? (Yes/No) [CRF – V0]
- If Yes, Informed Consent date (dd/mmm/yyyy) [CRF – V0]
- Visit date (dd/mmm/yyyy) [CRF – V0, V1, V2, V3, V4]
- Was surgery performed? (Yes/No) [CRF – V2]
- If Yes, date of surgery (dd/mm/yyyy) [CRF – V2]
- Has the patient completed the study? (Yes/No) [CRF – EOS]
- If Yes, specify date (dd/mm/yyyy) [CRF – EOS]
- If No, specify the reason for early termination or withdrawal (Screening failure/Consent withdrawal/Adverse event/Protocol violation/Lost to follow-up/Subject non-compliance/Death/Other) [CRF – EOS]
- Date of withdrawal (dd/mmm/yyyy) [CRF – EOS]
- If Death, please specify cause of death (free text) [CRF – EOS]
- If Other, please specify (free text) [CRF – EOS]

##### Derived Variables:

- Eligibility of the patient according to Inclusion/Exclusion criteria
- Date of study termination: the date of withdrawal or the date of study completion
- Whether the patient belongs to each different analysis sets and the reasons for exclusion from each set.


##### Imputations for missing values:

Not applicable.

|                               |          |              |
|-------------------------------|----------|--------------|
| Analysis Sets to be used for: | Tables   | All patients |
|                               | Listings | All patients |
|                               | Figures  | All patients |

Patients' data will be summarized as follows:

|  |  |
|--|--|
| <b>Table 1.</b> Disposition of the patients      | The total number of patients included in the different analysis and, in case of exclusion, reasons for exclusion from each analysis sets will be provided. |
| <b>Table 2.</b> Patients who completed the study | Frequencies tables of patients who completed the study. For patients who did not complete the study, reason of withdrawal will be provided.                |

|  |                           |                  |                |
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**Table 3.** Study status by visit      The number of patients taking part at each study visit will be provided.

Patients' data will be listed as follows:


**Listing 1A.** Disposition of the patients – Study participation      Listing of all patients with information about study participation: IC signature, eligibility, study termination status, eligibility in each dataset, and, if applicable, reason of exclusion from each dataset and/or of withdrawal.

**Listing 1B.** Disposition of the patients – Study dates      Listing of all patients and study dates of each step of the study: date of informed consent, visit dates, surgery date, study termination and/or withdrawal.

Patients' data will be represented as follows:

**Figure 1.** Disposition of the patients      The number of patients included in analyses data sets.

**Figure 2.** Status of study termination      The number of patients who completed the study as protocol and the number of patients who did not complete the study as protocol with withdrawal reason.

|  |                           |                  |                |
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### 6.1.2. Demographic and Other Baseline Characteristics

#### Collected Variables:

- Age (years) [CRF – V0]
- Ethnic group (Caucasian/Asian/Black/Other) [CRF – V0]
- If Other, please specify (free text) [CRF – V0]
- Smoking habits (Non-smoker/Former smoker/Smoker/Smoker with medical device) [CRF – V0]
- Alcohol abuse (Yes/No)
- If Yes, please specify (free text) [CRF – V0]
- Was urine pregnancy test performed? (Yes, No, Menopausal status, Surgery for sterility, Other) [CRF – CRF – V0]
- If no, please specify (free text) [CRF – V0]
- If Other, please specify (free text) [CRF – V0]
- If Yes: Date of pregnancy test (dd/mmm/yyyy) [CRF – V0]
- Result of pregnancy test (Positive/Negative) [CRF – V0]

#### Derived Variables:

Not applicable

#### Imputations for missing values:

Not applicable.


|                               |          |                 |
|-------------------------------|----------|-----------------|
| Analysis Sets to be used for: | Tables   | SAS             |
|                               | Listings | SAS             |
|                               | Figures  | Not applicable. |

Patients' data will be summarized as follows:

|  |   |
|--|---|
| <b>Table 4.</b> Baseline and demographic characteristics | Descriptive analyses of baseline and demographic characteristics of patients included in the SAS. |
|--|---|

Patients' data will be listed as follows:

|  |  |
|--|--|
| <b>Listing 2.</b> Baseline and demographic characteristics | Listing of all information about baseline and demographic characteristics collected for of SAS patients. |
|--|--|

|  |                           |                  |                |
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### 6.1.3. Protocol Violations

Protocol violations are major deviations from the procedures outlined in the protocol like missed evaluations, incorrect timing of evaluations, non-compliance with study medications and intake of medications not allowed or any non-adherence to the protocol that impacts patient's rights, safety or welfare, or/and that may affect the efficacy outcome or the treatment of the patients.

#### Collected Variables:

- Details of violation (free text) [External data]
- Violation category (free text) [External data]
- Violation type (free text) [External data]

#### Derived Variables:

Not applicable.

#### Imputations for missing values:

Not applicable.


|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | All patients   |
|                               | Listings | All patients   |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:

|                                     |   |
|-------------------------------------|---|
| <b>Table 5.</b> Protocol Violations | The number of patients included in the SAS presenting at least one protocol violation will be presented. Frequency table will be presented by type of protocol violation. Patients may have more than one protocol violation. |
|-------------------------------------|---|


Patients' data will be listed as follows:

|                                       |   |
|---------------------------------------|---|
| <b>Listing 3.</b> Protocol violations | Listing of all patients concerned by protocol deviations, details, and category and type of the deviation (minor or major, and whether it is causing exclusion from PPS). |
|---------------------------------------|---|

|  |                           |                  |                |
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#### 6.1.4. Compliance to Study Treatment

Not applicable for the study.

|   |                           |                  |                |
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### 6.1.5. Inclusion/Exclusion

The study specific Inclusion/Exclusion Criteria are presented in Section 2.6 of the Study Protocol. For each criterion, as appropriate, a response of “Yes/No” had to be obtained at Screening V0.


#### Collected Variables:

Inclusion criteria:

- 1. Patient Informed consent form (ICF) signed (Yes/No) [CRF – V0]
- 2. Female Aged  $\geq 18$  years at the time of the signature of ICF (Yes/No) [CRF – V0]
- 3. Histologic diagnosis of IBC or DCIS (Yes/No) [CRF – V0]
- 4. Tumor excision that will require localization because it cannot be definitively defined by palpation (Yes/No) [CRF – V0]
- 5. The tumor is unifocal; possible satellite lesions < 2 cm from primary are eligible (Yes/No) [CRF – V0]
- 6. The tumor enhances and is greater than or equal to 5mm on prone breast MRI imaging (Yes/No) [CRF – V0]
- 7. Subject and surgeon agree to perform BCS (Yes/No) [CRF – V0]
- 8. Willingness to follow all study procedures, including attending all site visits, tests and examinations (Yes/No) [CRF – V0]
- Were all inclusion criteria met? (Yes/No) [CRF – V0]

Exclusion criteria

- 1. Absolute contraindication to MRI, including presence of implanted electrical device (e.g., pacemaker or neurostimulator), aneurysm clip, or metallic foreign body in or near eyes (Yes/No) [CRF – V0]
- 2. Severe claustrophobia (Yes/No) [CRF – V0]
- 3. Contraindication to use of gadolinium-based intravenous contrast, including life-threatening allergy (Yes/No) [CRF – V0]
- 4. Uncontrolled cardiac, renal, or pulmonary disease (Yes/No) [CRF – V0]
- 5. Uncontrolled systemic disease (e.g., lupus erythematosus or scleroderma) (Yes/No) [CRF – V0]
- 6. Compromised renal function including chronic, severe kidney disease (GFR < 30 ml/min/1.73m<sup>2</sup>), or acute kidney injury (Yes/No) [CRF – V0]
- 7. Pregnancy or breast-feeding (Yes/No) [CRF – V0]
- 8. Subjects who have received or plan to receive neoadjuvant chemotherapy (Yes/No) [CRF – V0]
- 9. Sternal notch to nipple distance of > 32 cm as measured in a sitting or standing position (Yes/No) [CRF – V0]

|  |                           |                  |                |
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- 10. Measurement of widest circumference around breasts and arms > 135 cm (Yes/No) [CRF – V0]
- 11. Known allergy to device components (Yes/No) [CRF – V0]
- 12. Multicentric tumors (additional tumors > 2 cm from primary) (Yes/No) [CRF – V0]
- 13. Infectious or inflammatory processes near the area of intervention (Yes/No) [CRF – V0]
- 14. Planned surgery with localization devices including WGL, intraoperative ultrasound guidance, radiofrequency emitting implants, magnetic seeds, radioactive seeds, and tissue inspection devices (Yes/No) [CRF – V0]
- 15. Simultaneous participation in an interventional study or participation in an interventional study in the last 1 month before study inclusion (Yes/No) [CRF – V0]
- 15. Known drug and/or alcohol abuse (Yes/No) [CRF – V0]
- 16. Mental incapacity that precludes adequate understanding or cooperation (Yes/No) [CRF – V0]

For site 3:

- 15. Simultaneous participation in an interventional study or participation in an interventional study in the last 1 month before study inclusion, that, in the opinion of the Investigator, could impact patient's safety or the study endpoints (Yes/No) [CRF – V0]
- If no, Is the patient participating in another interventional study? (Yes/No) [CRF – V0]
- If Yes, please specify the interventional study (free text) [CRF – V0]
- Were any exclusion criteria met? (Yes/No) [CRF – V0]

#### Derived Variables:

Not applicable.


#### Imputations for missing values:

Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | All patients   |
|                               | Listings | All patients   |
|                               | Figures  | Not applicable |


Patients' data will be summarized as follows:

|                                    |  |
|------------------------------------|--|
| <b>Table 6.</b> Inclusion criteria | Frequencies table of patients who met or did not meet each inclusion criteria. |
| <b>Table 7.</b> Exclusion criteria | Frequencies table of patients who met or did not meet each exclusion criteria. |

|  |                           |                  |                |
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Patients' data will be listed as follows:

**Listing 4.** Inclusion and criteria      Listing of all patients with at least one exception to inclusion and exclusion criteria and details of the violated criteria.

|  |                           |                  |                |
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### 6.1.6. Medical History

Medical history is defined as any condition that the patient may have prior to enrollment in the study or, including any chronic conditions diagnosed prior to entry in the study. Medical history will be reported on a by-patient basis.

Medical history includes patient-reported bra cup size and documentation of any contraindications to MRI (e.g., implanted electrical devices exist) and history of adverse reactions to gadolinium.

#### Collected Variables:


- Examination performed? (Yes/No) [CRF – V0]
- If No, please specify (free text) [CRF – V0]
- Bra cup size (number) [CRF – V0]
- Contraindications to MRI? (Yes/No) [CRF – V0]
- If Yes, please specify (free text) [CRF – V0]
- History of adverse events to gadolinium? (Yes/No) [CRF – V0]
- If Yes, please specify (free text) [CRF – V0]

Classification of medical condition for Medical History:

1. Infections and infestations (Yes/No) [CRF – V0]
2. Neoplasms (including cysts and polyps) (Yes/No) [CRF – V0]
3. Cardiovascular disorders (Yes/No) [CRF – V0]
4. Immune system disorders (Yes/No) [CRF – V0]
5. Endocrine disorders (Yes/No) [CRF – V0]
6. Metabolism and nutrition disorders (Yes/No) [CRF – V0]
7. Nervous system disorders (Yes/No) [CRF – V0]
8. Ear and labyrinth disorders (Yes/No) [CRF – V0]
9. Respiratory, thoracic and mediastinal disorders (Yes/No) [CRF – V0]
10. Gastrointestinal disorders (Yes/No) [CRF – V0]
11. Hepatobiliary disorders (Yes/No) [CRF – V0]
12. Skin and sub-cutaneous tissue disorders (Yes/No) [CRF – V0]
13. Musculoskeletal and connective tissue disorders (Yes/No) [CRF – V0]
14. Renal and urinary disorders (Yes/No) [CRF – V0]
15. Reproductive system disorders (Yes/No) [CRF – V0]
16. Injury, poisoning and procedural complications (Yes/No) [CRF – V0]
17. Surgical procedures (Yes/No) [CRF – V0]
18. Other (Yes/No) [CRF – V0]
19. Other (Yes/No) [CRF – V0]

For each of the above:

- If Yes:

|  |                           |                  |                |
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- Specify (free text) [CRF – V0]
- Start date (mm/yyyy) [CRF – V0]
- End date (mm/yyyy) [CRF – V0]
- Ongoing (Yes/No) [CRF – V0]
- Ongoing (Yes/No) [CRF – V0]

#### **Derived Variables:**

Not applicable.

#### **Imputations for missing values:**

Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:


**Table 8A.** Medical history – General information      Frequencies table of general information concerning the examination of the condition of the patients included in the SAS.

**Table 8B.** Medical history – Previous and ongoing conditions      Frequencies table of previous and ongoing condition of the patients included in the SAS.

Patients' data will be listed as follows:

**Listing 5A.** Medical history – General information      Listing of general information concerning the examination of the conditions of the patients.

**Listing 5B.** Medical history – Previous and ongoing conditions      Listing of previous and ongoing condition of the patients.

|  |                           |                  |                |
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### 6.1.7. Trial Specific Diseases

All subjects were required to have a mammogram and prone MRI assessment prior to enrolment as per clinical practice. Results of imaging studies should have been obtained within 3 months of study enrolment. The results from pathological analysis of diagnostic core biopsy specimens (including IBC vs. DCIS) will be documented.

At V1, subjects underwent a supine MRI (10-40 days prior to surgery), which was used to generate a 3D breast image and determine the BCL.

#### Collected Variables:

Previous radiological assessment

- Was mammogram available prior to enrollment? (Yes/No) [CRF – V0]
- If No, please specify (free text) [CRF – V0]
- If Yes, was IBC/DCIS confirmed? (Yes/No) [CRF – V0]
- Was prone MRI available prior to enrollment? (Yes/No) [CRF – V0]
- If No, please specify (free text) [CRF – V0]
- Tumor maximal diameter (mm) (number) [CRF – V0]
- Presence of satellite lesions less than or equal to 2 cm from the primary? (Yes/No) [CRF – V0]
- Was pathological analysis of diagnostic core biopsy specimens available prior to enrollment? (Yes/No) [CRF – V0]
- If No, please specify (free text) [CRF – V0]
- If Yes, IBC or DCIS? (DCIS/IBC/Both DCIS and IBC) [CRF – V0]


Supine MRI

- Was supine MRI performed? (Yes/No) [CRF – V1]
- If No, please specify (free text) [CRF – V1]
- Where images transferred to CairnSurgical? (Yes/No) [CRF – V1]
- If no, reason (free text) [CRF – V1]
- Tumor maximum diameter (cm) (number) [CRF – V1]
- Tumor volume (cm<sup>3</sup>) (number) [CRF – V1]
- Optimal resection volume (cm<sup>3</sup>) (number) [CRF – V1]

#### Derived Variables:

Not applicable.

#### Imputations for missing values:

|  |                           |                  |                |
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Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:


|   |  |
|---|--|
| <b>Table 9.</b> Previous radiological assessments | Frequencies table of information and results about the previous radiological assessment of the patients included in the SAS. |
|---|--|

|                             |   |
|-----------------------------|---|
| <b>Table 10.</b> Supine MRI | Frequencies table of information and results collected through the supine MRI for the patients included in the SAS. |
|-----------------------------|---|

Patients' data will be listed as follows:

|   |  |
|---|--|
| <b>Listing 6.</b> Previous radiological assessments | Listing of information and results about the previous radiological assessment of the patients. |
|---|--|

|                              |  |
|------------------------------|--|
| <b>Listing 7.</b> Supine MRI | Listing of information and results collected through the supine MRI. |
|------------------------------|--|

|  |                           |                  |                |
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### 6.1.8. Prior and Concomitant Medications

#### Collected Variables:

- AE reference number (number) [CRF – CM cumulative form]
- Medication (free text) [CRF – CM cumulative form]
- Dose (number) [CRF – CM cumulative form]
- Units (free text) [CRF – CM cumulative form]
- Frequency (Once daily/ Twice daily/ 3 times daily/ 4 times daily/ 5 times daily/ As required/ Other/ NA) [CRF – CM cumulative form]
- Dosage (Tablet/ Capsule/ Ointment/ Suppository/ Aerosol/ Suspension/ Spray/ Patch/ Syrups/ Drops/ Vials/ Gel/ Cream/ Other/ NA) [CRF – CM cumulative form]
- Route (Oral/ intravenous/ Subcutaneous/ Intramuscular/ Inhalation/ Topical/ Sublingual/ Other/ NA) [CRF – CM cumulative form]
- Indication (free text) [CRF – CM cumulative form]
- Start date (dd/mm/yyyy) [CRF – CM cumulative form]
- End date (dd/mm/yyyy) [CRF – CM cumulative form]
- Ongoing (Yes/No) [CRF – CM cumulative form]

#### Derived Variables:

- **Prior medications** are defined as those starting and ending prior to the first administration of investigational study medication.
- **Concomitant medications** are defined as:
  - o The start date on or after the study treatment start date  
OR
  - o The start date before the study treatment start date AND the stop date after or on the study treatment start date.  
OR
  - o The start date before the study treatment start date AND the stop date missing AND the tick box "Ongoing" marked.


#### Imputations for missing values:

Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:

**Table 11.** Prior                      The number of patients with at least one prior medication will be presented

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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medications

by indication and active principle, where the percentage of patients is calculated relative to the total number of patients considered valid for the SAS.


**Table 12.** Concomitant medications

The number of patients with at least one concomitant medication will be presented by indication and active principle, where the percentage of patients is calculated relative to the total number of patients considered valid for the SAS.

Patients' data will be listed as follows:

**Listing 7.** Prior and concomitant medications

Listing of information about prior and concomitant medications for SAS patients.

|  |                           |                  |                |
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## 6.2. Efficacy Analysis

At V2, surgery utilizing the BCL was performed. On the same day, the volume of the excised specimen was measured, and the specimen was sent to the pathology lab for analysis. Results, including the positive margin rate (PMR) and specimen mammogram findings, were obtained within 14 days.

### 6.2.1. Primary Efficacy Analysis

To assess the performance of BCL in minimizing positive margin rates, the proportion of patients with positive margins after partial mastectomy with BCL will be measured. Information regarding the surgery and the related procedures, the presence of positive margins and the procedures used to evaluate the endpoint are outlined in the following section.

#### Collected Variables:

- Was surgery performed? (Yes/No) [CRF –V2]
- If No, please specify the reason (free text) [CRF –V2]  
If Yes:
- Date of surgery (dd-mmm-yyyy) [CRF –V2]
- Was Tumor specimen removed? (Yes/No) [CRF –V2]
- If No, please specify the reason (free text) [CRF –V2]  
If Yes:
- Was specimen mammogram obtained? (Yes/No) [CRF –V2]
- If No, please specify the reason (free text) [CRF –V2]
- Was tumor specimen sent to the pathologist for evaluation of the positive margins? (Yes/No) [CRF –V2]
- If No, please specify the reason (free text) [CRF –V2]
- Were positive margins detected? (Yes/No) [CRF –V2]

#### Derived Variables:

Not applicable.


#### Analysis of Primary Efficacy variable:

To evaluate the performance of BCL in reducing the positive margin rate, exact . 95% Confidence Interval (CI) for positive margin rate (PMR) using the Clopper-Pearson method will be estimated with actual positive margin rate calculated at V2

The primary analysis will be performed on both FAS and PPS. The analysis performed on PPS will be obtained to support the results on FAS.

Moreover, bar plots will be presented to show the positive margin rate distribution.

#### Imputations for missing values:

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | FAS, PPS       |
|                               | Listings | FAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:


|   |   |
|---|---|
| <b>Table 14.</b> Surgery and positive margin evaluation | Frequency table of information about the surgery and the related procedures, tumor specimen handling, and evaluation of the presence of positive margins for patients in FAS and PPS. |
|---|---|

Patients' data will be listed as follows:

|  |   |
|--|---|
| <b>Listing 8.</b> Surgery and positive margin evaluation | Listing of all information the surgery and the related procedures, tumor specimen handling, and evaluation of the presence of positive margins for patients in FAS and PPS. |
|--|---|

Patients' data will be represented as follows:

|                                   |   |
|-----------------------------------|---|
| <b>Figure 3.</b> Positive margins | Bar plot displaying the proportion of patients with positive margins after surgery with BCL in FAS and PPS, respectively. |
|-----------------------------------|---|

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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## 6.2.2. Analysis of Secondary Variables

The analysis of the following secondary endpoint will be described in this section.

The secondary endpoints are defined as follows:

- To calculate the specimen volume after BCL guided partial mastectomy, the water displacement method (WDM) will be used (results will be obtained within the same day of surgery).
- To compare the ideal specimen volume to the actual specimen volume and tumor volume, the tumor maximum diameter (mm) and tumor volume (mm<sup>3</sup>) on supine MRI, and the ideal specimen volume (mm<sup>3</sup>) will be recorded at V1;
- To record important clinical data on the removed specimens the presence of invasive cancer in core biopsy (Y/N), presence of DCIS in core biopsy (Y/N), presence of invasive cancer in lumpectomy specimen (Y/N), presence of DCIS in lumpectomy specimen (Y/N), subtype of invasive cancer (ductal vs lobular vs other), maximal tumor diameter (mm) on pathology report of lumpectomy specimen, shave biopsy done during surgery (Y/N and if done how many) will be recorded and checked.
- To evaluate the surgeon's perception of ease of use of the BCL system, a 5 Likert scale will be used at V2;
- To evaluate the patient's satisfaction, the BREAST-Q will be used at EOS/V4;
- To evaluate the safety and tolerability of BCL through physical examination and AEs assessment including the relationship of the AE to the BCL system at V1, V2, V3, V4.

### Collected Variables:

#### *Specimen and tumor volumes*

- Specimen volume determined by water displacement (ml) (number) [CRF –V2]
- Maximal tumor diameter on pathology report of lumpectomy specimen (cm) (number) [CRF –V2]


#### *Shave biopsies*

- Were any shave biopsies done? (Yes/No) [CRF –V2]
- If Yes, how many (number) [CRF –V2]
- What is the volume of shave biopsy determined by water displacement? (ml) (number) [CRF –V2]

#### *Cancer Characteristics in Biopsy and Lumpectomy*

- IBC or DCIS in lumpectomy specimen? (DCIS/IBC/Both) [CRF –V2]
- If invasive, subtype (Ductal/Lobular/Other) [CRF –V2]
- If other, please specify (free text) [CRF –V2]


#### *Likert Questionnaire for Ease of Use of BCL*

|  |                           |                  |                |
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- Did the investigator complete the Likert questionnaire? (Yes/No) [CRF – V2]
- If No, please specify the reason (free text) [CRF – V2]
- If Yes:
- 1. Overall, how satisfied or dissatisfied are you with the BCL device? (Very satisfied/Somehow satisfied/Neither satisfied nor dissatisfied/Somehow dissatisfied/Very dissatisfied) [CRF – V2]
- 2. How would you rate the ease of use of the BCL device? (Very easy/Easy/Neither easy nor complicated/Complicated/Very complicated) [CRF – V2]
- 3. How much, in your opinion, has the BCL device simplified surgery? (Very much/Somewhat/Neutral/Not really/Not at all) [CRF – V2]
- 4. How much, in your opinion, did the BCL device speed up surgery? (Very much/Somewhat/Neutral/Not really/Not at all) [CRF – V2]
- 5. How would you rate the safety of the BCL device? (Very high/High/Neither high nor low/Low/Very low) [CRF – V2]
- 6. How would you rate the reliability of the BCL device? (Very high/High/Neither high nor low/Low/Very low) [CRF – V2]
- 7. How likely would you be to reuse the BCL device? (Very likely/Likely/Neither likely nor unlikely/Unlikely/Very unlikely) [CRF – V2]
- 8. How likely would you be to recommend the use of the BCL device to your colleagues? (Very likely/Likely/Neither likely nor unlikely/Unlikely/Very unlikely) [CRF – V2]

#### *Likert Questionnaire for the Visualizer*

- Did the investigator complete the Likert questionnaire? (Yes/No) [CRF – V2]
- If No, please specify the reason (free text) [CRF – V2]
- If Yes:
- 1. Overall, how satisfied or dissatisfied are you with the Visualizer? (Very satisfied/Somehow satisfied/Neither satisfied nor dissatisfied/Somehow dissatisfied/Very dissatisfied) [CRF – V2]
- 2. How would you rate the clarity of the 3D tumor image created by the Visualizer? (Very high/High/Neither high nor low/Low/Very low) [CRF – V2]
- 3. How would you rate the reliability of the 3D tumor image created by the Visualizer? (Very high/High/Neither high nor low/Low/Very low) [CRF – V2]
- 4. How would you rate the ease of use of the Visualizer? (Very easy/Easy/Neither easy nor complicated/Complicated/Very complicated) [CRF – V2]
- 5. How much, in your opinion, did the Visualizer help surgery? (Very much/Somewhat/Neutral/Not really/Not at all) [CRF – V2]
- 6. How much, in your opinion, did the Visualizer speed up surgery? (Very much/Somewhat/Neutral/Not really/Not at all) [CRF – V2]
- 7. How likely would you be to reuse the Visualizer? (Very likely/Likely/Neither likely nor unlikely/Unlikely/Very unlikely) [CRF – V2]
- 8. How likely would you be to recommend the use of the Visualizer to your colleagues? (Very likely/Likely/Neither likely nor unlikely/Unlikely/Very unlikely) [CRF – V2]

|  |                           |                  |                |
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### *BREAST-Q*

- Did the subject complete the BREST-Q questionnaire? (Yes/No) [CRF – V4]
- If No, please specify the reason (free text) [CRF – V4]


If Yes:

#### *BREAST CANCER CORE SCALE (PREOPERATIVE): SATISFACTION WITH BREASTS:*

- A. How you look in the mirror clothed? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- B. How comfortably do your bras fit? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- C. Being able to wear clothing that is more fitted? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- D. How you look in the mirror unclothed? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]

#### *BCT MODULE (POSTOPERATIVE): SATISFACTION WITH BREASTS:*

- A. How you look in the mirror clothed? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- B. The shape of your lumpectomy breast when you are wearing a bra? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- C. How normal you feel in your clothes? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- D. Being able to wear clothing that is more fitted? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- E. How your lumpectomy breast sits/hangs? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- F. How smoothly shaped your lumpectomy breast looks? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- G. The contour (outline) of your lumpectomy breast? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- H. How equal in size your breasts are to each other? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- I. How normal your lumpectomy breast looks? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- J. How much your breasts look the same? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]
- K. How you look in the mirror unclothed? (Very dissatisfied/Somewhat dissatisfied/Somewhat satisfied/Very satisfied) [CRF – V4]


|  |                           |                  |                |
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### Derived Variables:

- Breast-Q score as foreseen by the scale's user's manual.

Sum of all items scores will be calculated for both preoperative and postoperative BREAST-Q module and converted into an equivalent RASCH transformed score (0-100). Higher scores reflect a better outcome.

| MODULE        | SUM SCORE | EQUIVALENT RASCH TRANSFORMED SCORE (0-100) |
|---------------|-----------|--|
| Preoperative  | 4         | 0  |
|               | 5         | 23   |
|               | 6         | 29   |
|               | 7         | 34   |
|               | 8         | 39   |
|               | 9         | 44   |
|               | 10        | 48   |
|               | 11        | 53   |
|               | 12        | 58   |
|               | 13        | 64   |
|               | 14        | 71   |
|               | 15        | 82   |
|               | 16        | 100  |
| Postoperative | 11        | 0  |
|               | 12        | 15   |
|               | 13        | 20   |
|               | 14        | 24   |
|               | 15        | 26   |
|               | 16        | 29   |
|               | 17        | 31   |
|               | 18        | 33   |
|               | 19        | 35   |
|               | 20        | 36   |
|               | 21        | 38   |
|               | 22        | 40   |
|               | 23        | 42   |
|               | 24        | 43   |
|               | 25        | 45   |
|               | 26        | 46   |
|               | 27        | 48   |
|               | 28        | 50   |
|               | 29        | 51   |
|               | 30        | 53   |
|               | 31        | 55   |
|               | 32        | 57   |
|               | 33        | 59   |
|               | 34        | 61   |
|               | 35        | 63   |
|               | 36        | 65   |
|               | 37        | 67   |
|               | 38        | 69   |
|               | 39        | 72   |
|               | 40        | 75   |

|  |                           |                  |                |
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|  |    |     |
|--|----|-----|
|  | 41 | 78  |
|  | 42 | 82  |
|  | 43 | 88  |
|  | 44 | 100 |

## Analysis of Secondary Efficacy variables

### *Tumour and specimen measures*

The specimen volume after BCL-guided partial mastectomy was determined using the water displacement method, with results recorded on the same day as the surgery (Visit V2). Summary statistics will be calculated for the specimen volume, as well as for the maximal tumor diameter on the pathology report of the lumpectomy specimen (cm). The results will be presented in tables, along with tumor volumes and the ideal specimen volume derived from preoperative imaging for comparative purposes, and box plots will be used to visualize differences and variability in volumes.

### *Shave biopsies*

The number and volume of shave biopsies taken during BCL-guided partial mastectomy was recorded on the day of surgery (Visit V2). The specimen volume for each shave biopsy was determined using the water displacement method. Frequencies for the number of shave biopsies and summary statistics of their respective volumes will be calculated. (Secondary endpoint 3).

### *Cancer Characteristics in Biopsy and Lumpectomy*


Important clinical characteristics of the removed specimens will be analyzed, including the presence of invasive cancer (IBC) or ductal carcinoma in situ (DCIS) in core biopsies and lumpectomy specimens. The frequency and percentages of each classification will be summarized, along with invasive cancer subtypes (ductal, lobular, or other).

### *Surgeon's perception of ease of use of the BCL system and Visualizer*

Responses to the investigator-administered Likert questionnaire assessing the ease of use of the BCL device will be analyzed descriptively. The frequencies and percentages for each response category (e.g., "Very satisfied," "Satisfied") will be reported for all items, including overall satisfaction, ease of use, safety, reliability, and likelihood of reuse or recommendation. Results will be displayed in summary tables and listings.

The investigator's satisfaction with the Visualizer system will be analyzed using responses to a separate Likert questionnaire. Frequencies and percentages for each response will be summarized for items assessing clarity, reliability, ease of use, and the system's impact on surgical assistance and time. These results will be tabulated and listed for individual responses. (Secondary endpoint 4).

### *Patient Satisfaction (BREAST-Q Assessment)*

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Patient-reported satisfaction will be evaluated using the BREAST-Q questionnaire. The scores of each answer range from 1 (worst answer) to 4 (best answer): the raw total scores for each module (preoperative and postoperative) will be calculated, then converted to Rasch scores (0–100) as per the BREAST-Q user's manual. Higher scores reflect greater satisfaction. Missing data will be imputed with the means of completed items if less than 50% of the scale items are missing, as per the manual guidelines. Results will be summarized in tables and figures, including a box plot of Rasch scores for visual comparison.

The evaluation of the secondary endpoint related to the assessment of the safety and tolerability of BCL, including physical examination and the assessment of adverse events (AEs) — as well as the relationship between the AEs and the BCL system — will be outlined in section 6.4, Safety Variables.


### Imputations for missing values:

For breast-Q, as foreseen by scale users' manual, if missing data is less than 50% of the scale's items, the mean of the completed items will be inserted instead of the missing scores.

|                               |          |     |
|-------------------------------|----------|-----|
| Analysis Sets to be used for: | Tables   | FAS |
|                               | Listings | FAS |
|                               | Figures  | FAS |

Patients' data will be summarized as follows:

|  |   |
|--|---|
| <b>Table 14.</b> Specimen and tumor volumes                      | Summary statistics for specimen and tumor measurements collected at different stages of the study, including pre-surgery (Supine MRI) and post-surgery (after Surgery at V2). |
| <b>Table 15.</b> Shave biopsies                                  | Frequency and number of shave biopsies performed, along with the summary statistics of volume of the biopsy specimens determined by water displacement                        |
| <b>Table 16.</b> Cancer characteristics in biopsy and lumpectomy | Frequency of cases identified as IBC, DCIS, or both, based on core biopsy and lumpectomy specimen results, and details of subtype classifications for invasive cases.         |
| <b>Table 17.</b> Likert questionnaire for ease of use of BCL     | Frequencies of responses to each item on the Likert-scale questionnaire administered to the investigator regarding the ease of use of BCL.                                    |
| <b>Table 18.</b> Likert questionnaire the                        | Frequencies of responses to each item on the Likert-scale questionnaire administered to the investigator regarding the satisfaction towards the                               |

|  |                           |                  |                |
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Visualizer

Visualizer.

**Table 19.** Breast-Q


Frequencies of responses to all items of the BREAST-Q and summary statistics of the raw and RASCH converted score, as completed by the patients.

Patients' data will be listed as follows:

- |  |   |
|--|---|
| <b>Listing 10.</b> Specimen volumes                                | Listing of specimen and tumor measurements, including volumes collected pre-surgery (via supine MRI) and post-surgery (at visit V2).                        |
| <b>Listing 11.</b> Shave biopsies                                  | Listing of information on shave biopsies, number of shave biopsies performed, along with volume of the biopsy specimens determined by water displacement.   |
| <b>Listing 12.</b> Cancer characteristics in biopsy and lumpectomy | Listing of classification of cases identified as IBD, DCIS or both, and details of subtype classifications for invasive cases.                              |
| <b>Listing 13.</b> Likert questionnaire for ease of use of BCL     | Listing of Individual responses to all items from the Likert-scale questionnaire on the ease of use of the BCL system, as completed by investigators.       |
| <b>Listing 14.</b> Likert questionnaire for the Visualizer         | Listing of Individual responses to all items from the Likert-scale questionnaire on satisfaction with the Visualizer system, as completed by investigators. |
| <b>Listing 15A.</b> Breast-Q – pre-operative module                | Listing of Individual responses to all items from the pre-operative BREAST-Q and score, as completed by the patients.                                       |
| <b>Listing 15B.</b> Breast-Q – post-operative module               | Listing of Individual responses to all items from the post-operative BREAST-Q and score, as completed by the patients.                                      |

Patients' data will be represented as follows:

- |   |  |
|---|--|
| <b>Figure 4.</b> Tumor and specimen volumes | Box plot displaying the distribution of tumor and specimen volumes measures gathered across different stages of the study. |
| <b>Figure 5.</b> Tumor classification       | Bar chart displaying the cases identified as IBD, DCIS or both, and details of subtype classifications for invasive cases. |


|  |                           |                  |                |
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**Figure 6.** BREAST-Q scores

Box plot displaying the distribution of BREAST-Q Rasch scores from pre and post operative modules.


### 6.2.3. Analysis of Other Variables

Not applicable.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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### 6.3. Dispensing and collection of diaries, questionnaires, and kits

Not applicable for this study.

|  |                           |                  |                |
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## 6.4. Safety Variables

### 6.4.1. Adverse Events


#### Collected Variables:

- AE reference number (number) [CRF – AE cumulative form]
- Event (free text) [CRF – AE cumulative form]
- Start date (dd/mm/yyyy) [CRF – AE cumulative form]
- End date (dd/mm/yyyy) [CRF – AE cumulative form]
- Ongoing status (Yes/No) [CRF – AE cumulative form]
- Outcome (Recovered or Resolved/Recovered or Resolved with residual effects/Recovering or Resolving/Not recovered or Not resolved/Fatal/Unknown) [CRF – AE cumulative form]
- Severity (Mild/Moderate/ Severe or medically significant/ Life-threatening consequences or urgent intervention indicated/ Death related to AE) [CRF – AE cumulative form]
- Treatment (None/Drug treatment/Other (e.g. Procedure/surgery) [CRF – AE cumulative form]
- Causal relationship (Not related, Possible, Probable, Causal relationship) [CRF – AE cumulative form]
- Action taken (None, Study discontinuation) [CRF – AE cumulative form]
- Seriousness (Not serious/Serious) [CRF – AE cumulative form]

#### Derived Variables:

- PT, LLT and SOC term applying MedDRA® dictionary;
- Adverse Events (AEs): An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in patients, users or other parties, whether or not related to the investigational product; this definition includes events related to:
  - the investigational product
  - the procedure involved
- Serious adverse events (SAEs): Adverse events that
  - a) led to death,
  - b) led to serious deterioration in the health of the patient, resulting in
    - 1) a life-threatening illness or injury, or
    - 2) a permanent impairment of a body structure or a body function, or
    - 3) in-patient or prolonged hospitalization, or
    - 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
    - 5) fetal distress, fetal death or a congenital abnormality or birth defect

Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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In the analysis serious adverse events will be identified by the variables "Seriousness" (yes, no).

- Related AEs: in the analysis related AEs will be defined as AEs for which the relationship with study device is assessed as "none", "unlikely", "possible", "probable" or "definitive"
- Severe AEs: in the analysis severe AEs will be defined as AEs for which the severity is assessed as "severe" or "life threatening"
- Patients who prematurely terminated the Study Due to AE: in the analysis patients who prematurely terminated the study due to AE are defined as those patients with an adverse event for which the reason for early termination in the CRF end of study has been recorded as "adverse event"
- Death: death is defined as a fatal outcome of an AE.

Adverse events (AEs) will be reported on a per-patient basis. This implies that even if a patient reported the same event repeatedly, the event will be counted only once. In the latter case, the event will be assigned the worst severity and strongest relationship to the investigational study medication. The presentation of AEs is therefore restricted to the incidence per patient of AEs assigned to the Treatment Period.


#### **Imputations for missing values:**

Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:

|   |  |
|---|--|
| <b>Table 20A.</b> Summary of adverse events – AE occurrence | <p>Overview of AEs including the number of patients with:</p> <ul style="list-style-type: none"> <li>- number of patients with at least one AE.</li> <li>- number of patients with at least one device-related AE.</li> <li>- number of patients with at least one serious AE.</li> <li>- number of patients with at least one severe AE.</li> <li>- number of patients who prematurely terminated the study due to an AE</li> <li>- number of AEs</li> <li>- number of serious AEs</li> <li>- number of related AEs</li> <li>- number of severe AEs</li> <li>- number of deaths.</li> </ul> |
|---|--|

|  |                           |                  |                |
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**Table 20.** Summary of adverse events - MedDRA coding      Incidence of AEs , with frequency table by SOC and PT name.

**Table 21.** Incidence of AEs by relationship with IP      Incidence of AEs by relationship with IP by SOC and PT. A default frequency table will be presented for all the patients included in the SAS.

**Table 22.** Incidence of AEs by severity      Incidence of AEs by severity, SOC and PT. A default frequency table will be presented.


**Table 23.** Incidence of SAEs      Incidence of AEs by seriousness, SOC and PT. A default frequency table will be presented.

**Table 24.** Incidence of AEs leading to study termination      Incidence of AEs leading to study termination by SOC and PT. A default frequency table will be presented.

**Table 25.** Incidence of deaths      Incidence of deaths. A default frequency table will be presented.

Patients' data will be listed as follows:

**Listing 16.** Adverse events      Listing of all information about adverse events occurred during the study.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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#### 6.4.2. Clinical Laboratory Evaluation

Laboratory Tests include:

- serum creatinine levels to calculate the glomerular filtration rate (GFR), acid uric for renal dysfunction;
- complete blood count;
- electrolytes (sodium, potassium, chloride, bicarbonate).

##### Collected Variables:

- Was blood sampling performed? (Yes/No) [CRF – V0]
- If No, specify the reason (free text) [CRF – V0]
- If Yes:
- Date of blood sampling (dd-mmm-yyyy) [CRF – V0]

For each blood parameter (hemoglobin, hematocrit, red blood cells (RBC), platelets (PLT), white blood cells (WBC), neutrophil granulocytes, eosinophilic granulocytes, basophilic granulocytes, lymphocytes, monocytes, sodium, potassium, chloride, bicarbonate, serum creatinine, glomerular filtration rate (GFR), acid uric):

- Done? (Yes/No) [CRF – V0]
- Value (number) [CRF – V0]
- Unit (free text) [CRF – V0]
- Lower Normal Range (LNR) [CRF – V0]
- Upper Normal Range (UNR) [CRF – V0]
- Out of range (No/Yes – Clinically Relevant/Yes – Not Clinically Relevant) [CRF – V0]

##### Derived Variables:


Not applicable.

##### Imputations for missing values:

Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |


Patients' data will be summarized as follows:

|   |                           |                  |                |
|---|---------------------------|------------------|----------------|
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**Table 26.** Clinical Laboratory Evaluation. Descriptive statistics of all parameters of clinical laboratory evaluation for patients included in the SAS.

Patients' data will be listed as follows:

**Listing 17.** Clinical laboratory evaluation results Listing of all information about clinical laboratory evaluation results on laboratory evaluation results all parameters for patients included in the SAS.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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### 6.4.3. Vital Signs

#### Collected variables:

Only at V2:

- Examination performed within 10-40 days from supine MRI? (Yes/No) [CRF – V2]
- If No, please clarify the reason (free text) [CRF – V2]
- Examination performed prior to discharge? (Yes/No) [CRF – V2]
- If No, please clarify the reason: (free text)

For all visits, and for V2 before and after surgery:

- Examination performed? (Yes/No) [CRF –V0, V1, V2, V3]
- If No, please clarify the reason (free text) [CRF –V0, V1, V2, V3]

If Yes:

- Systolic Blood Pressure (SBP) (mmHg) [CRF –V0, V1, V3]
- Diastolic Blood Pressure (DBP) (mmHg) [CRF – V0, V1, V2, V3]
- Heart Rate (HR) (beats/min) [CRF – V0, V1, V2, V3]
- O<sub>2</sub> saturation (%) [CRF – V0, V1, V2, V3]

#### Derived Variables:

- For V2, variable identifying if the results regards pre or post-surgery
- Examination performed within 10-40 days from supine MRI/ prior to discharge will be displayed in a single variable

#### Imputations for missing values:

Not applicable.


|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:

**Table 16.** Vital signs      Descriptive statistics of vital signs-related values by study visit of Patients included in the SAS by visit

Patients' data will be listed as follows:

**Listing 18.** Vital signs      Listing of all information about vital signs of SAS patients by study visit.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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#### 6.4.4. Physical examination findings

A physical examination of the patients was carried out at V0, V2 (after discharge) and V3. Physical examination includes weight, height, distance from sternal notch to the nipple, the circumference around the breast and arms, calculation of BMI, and specific documentation that the breast cancer cannot be palpated.

##### Collected variables:

- Examination performed? (Yes/No) [CRF – V0, V2, V3]
- If No, please clarify the reason (free text) [CRF – V0, V2, V3]
- If Yes:
  - Weight (kg) (number) [CRF – V0, V2, V3]
  - Height (cm) (number) [CRF – V0, V2, V3]
  - BMI (kg/m<sup>2</sup>) (number) [CRF – V0, V2, V3]
  - Distance from sternal notch to the nipple (cm) (number) [CRF – V0, V2, V3]
  - Circumference around the breast and arms (cm) (number) [CRF – V0, V2, V3]
  - Specific documentation that the breast cancer cannot be palpated (free text) [CRF – V0, V2, V3]
  - Other abnormalities, if any (free text) [CRF – V0, V2, V3]

##### Derived Variables:

Not applicable.

##### Imputations for missing values:


Not applicable.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:


|   |   |
|---|---|
| <b>Table 19.</b> Physical examination results | Summary statistics of physical examination findings will be provided for all patients included in SAS by study visit. |
|---|---|

Patients' data will be listed as follows:

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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**Listing 19.** Physical examination results

Listing of all information about physical examination of SAS patients by study visit.

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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#### 6.4.5. Other Safety-Related Observations

Device deficiency is any inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Device Deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the Manufacturer including labelling.

##### Collected Variables:

- Any DEVICE DEFICIENCIES occurred during IP utilization? [CRF –V1, V2]
- If Yes, please clarify the reason (free text) [CRF –V1, V2]

##### Derived Variables:

Not applicable for this study.

##### Imputations for missing values:

Not applicable for this study.

|                               |          |                |
|-------------------------------|----------|----------------|
| Analysis Sets to be used for: | Tables   | SAS            |
|                               | Listings | SAS            |
|                               | Figures  | Not applicable |

Patients' data will be summarized as follows:


|                                      |   |
|--------------------------------------|---|
| <b>Table 20.</b> Device deficiencies | Counts and percentages of Device Deficiencies will be provided for all Patients included in SAS by study visit. |
|--------------------------------------|---|

Patients' data will be listed as follows:

|  |  |
|--|--|
| <b>Listing 29.</b> Device deficiencies | Listing of all Device Deficiencies by study visits for SAS patients. |
|--|--|


#### 6.5. Pharmacokinetic (PK)/ Pharmacodynamic (PD)

Not applicable for this study.

|   |                           |                  |                |
|---|---------------------------|------------------|----------------|
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## 6.6. Interim Analysis

Not applicable for this study.

|  |                           |                  |                |
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## 7. Changes to the Analysis as Laid Down in the Protocol and Amendments

No changes have been made to the analysis methods or procedures as specified in the protocol and subsequent amendments.

|   |                           |                  |                |
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## 8. Reference bibliography


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2. R. J. Barth et al., "A Patient-Specific 3D-Printed Form Accurately Transfers Supine MRI-Derived Tumor Localization Information to Guide Breast-Conserving Surgery," Annals of Surgical Oncology, vol. 24, no. 10, pp. 2950–2956, Oct. 2017, doi: 10.1245/s10434-017-5979-z.

|  |                           |                  |                |
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## 9. Tables, Listings and Figures layouts

### 9.1. Tables


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**Table 1. Disposition of the patients**

**All patients**


|   |              | <b>All patients<br/>(N=XX)</b> |
|---|--------------|--------------------------------|
| <b>Included in SAS</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason of exclusion</b>  |              |                                |
| <b>Screening failure</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason X</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>Included in SAS</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason of exclusion</b>  |              |                                |
| <b>Screening failure</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason X</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>Included in PPS</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason of exclusion</b>  |              |                                |
| <b>Screening failure</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason X</b>   | <b>N (%)</b> | X (XX.X)                       |
| SAS: Safety Analysis Set<br>FAS: Full Analysis Set<br>PPS: Per Protocol Set |              |                                |

|   |                           |                  |                |
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**Table 2. Patients who completed the study**

**All patients**


|  |              | <b>All patients<br/>(N=XX)</b> |
|--|--------------|--------------------------------|
| <b>Did the patient complete the study?</b> |              |                                |
| <b>Yes</b>                                 | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>                                  | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason of withdrawal</b>                |              |                                |
| <b>Reason X</b>                            | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason X</b>                            | <b>N (%)</b> | X (XX.X)                       |
| <b>Reason X</b>                            | <b>N (%)</b> | X (XX.X)                       |

|   |                           |                  |                |
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**Table 3. Study status by visit**

**All patients**


| Study visit       |       | All patients<br>(N=XX) |
|-------------------|-------|------------------------|
| Screening V0      | N (%) | X (XX.X)               |
| V1                | N (%) | X (XX.X)               |
| Surgery V2        | N (%) | X (XX.X)               |
| Follow-up V3      | N (%) | X (XX.X)               |
| EOS V4            | N (%) | X (XX.X)               |
| EOS: End Of Study |       |                        |

|  |                           |                  |                |
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**Table 4. Baseline and demographic characteristics**

**Safety Analysis Set**

|                                       |                  | <b>SAS<br/>(N=XX)</b> |
|---------------------------------------|------------------|-----------------------|
| <b>Age (years)</b>                    | <b>Mean ± SD</b> | XX ± X                |
|                                       | <b>Min - max</b> | XX - X                |
|                                       | <b>Missing</b>   | X                     |
| <b>Ethnic group</b>                   |                  |                       |
| <b>Caucasian</b>                      | <b>N (%)</b>     | X (XX.X)              |
| <b>Asian</b>                          | <b>N (%)</b>     | X (XX.X)              |
| <b>Black</b>                          | <b>N (%)</b>     | X (XX.X)              |
| <b>Other</b>                          | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>                        | <b>N</b>         | X                     |
| <b>Smoking habits</b>                 |                  |                       |
| <b>Non-smoker</b>                     | <b>N (%)</b>     | X (XX.X)              |
| <b>Former smoker</b>                  | <b>N (%)</b>     | X (XX.X)              |
| <b>Smoker</b>                         | <b>N (%)</b>     | X (XX.X)              |
| <b>Smoker with medical device</b>     | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>                        | <b>N</b>         | X                     |
| <b>Alcohol abuse</b>                  |                  |                       |
| <b>Yes</b>                            | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>                             | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>                        | <b>N</b>         | X                     |
| <b>Urine pregnancy test performed</b> |                  |                       |
| <b>Yes</b>                            | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>                             | <b>N (%)</b>     | X (XX.X)              |
| <b>Menopausal status</b>              | <b>N (%)</b>     | X (XX.X)              |
| <b>Surgery for sterility</b>          | <b>N (%)</b>     | X (XX.X)              |
| <b>Other</b>                          | <b>N (%)</b>     | X (XX.X)              |

|   |                           |                  |                |
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|  |              | <b>SAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>Missing</b>                                     | <b>N</b>     | X                     |
| <b>Result of pregnancy test</b>                    |              |                       |
| <b>Positive</b>                                    | <b>N (%)</b> | X (XX.X)              |
| <b>Negative</b>                                    | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>                                     | <b>N</b>     | X                     |
| SD: Standard Deviation<br>SAS: Safety Analysis Set |              |                       |

|   |                           |                  |                |
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**Table 5. Protocol violations**

**All patients**


| Patients with at least:                        |       | All patients<br>(N=XX) |
|--|-------|------------------------|
| One minor deviation                            |       |                        |
| Yes  | N (%) | X (XX.X)               |
| No   | N (%) | X (XX.X)               |
| One major deviation                            |       |                        |
| Yes  | N (%) | X (XX.X)               |
| No   | N (%) | X (XX.X)               |
| One major deviation causing exclusion from PPS |       |                        |
| Yes  | N (%) | X (XX.X)               |
| No   | N (%) | X (XX.X)               |
| PPS: Per Protocol Set                          |       |                        |

|  |                           |                  |                |
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**Table 6. Inclusion Criteria**

**All patients**


|  |              | <b>All patients<br/>(N=XX)</b> |
|--|--------------|--------------------------------|
| <b>Any inclusion criterion not met</b>   |              |                                |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>INCL. 1</b>   |              |                                |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>INCL. X</b>   |              |                                |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)                       |
| <p>Inclusion criteria:</p> <ol style="list-style-type: none"> <li>1. Patient Informed consent form (ICF) signed</li> <li>2. Female Aged = 18 years at the time of the signature of ICF</li> <li>3. Histologic diagnosis of IBC or DCIS</li> <li>4. Tumor excision that will require localization because it cannot be definitively defined by palpation</li> <li>5. The tumor is unifocal; possible satellite lesions &lt; 2 cm from primary are eligible</li> <li>6. The tumor enhances and is greater than or equal to 5mm on prone breast MRI imaging</li> <li>7. Subject and surgeon agree to perform BCS</li> <li>8. Willingness to follow all study procedures, including attending all site visits, tests and examinations</li> </ol> |              |                                |

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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**Table 7. Exclusion Criteria**

**All patients**


|   |              | <b>All patients<br/>(N=XX)</b> |
|---|--------------|--------------------------------|
| <b>Any exclusion criterion met</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>EXCL. 1</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <b>EXCL. X</b>  |              |                                |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)                       |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)                       |
| <p>Exclusion criteria</p> <ol style="list-style-type: none"> <li>Severe claustrophobia</li> <li>Contraindication to use of gadolinium-based intravenous contrast, including life-threatening allergy</li> <li>Uncontrolled cardiac, renal, or pulmonary disease</li> <li>Uncontrolled systemic disease (e.g., lupus erythematosus or scleroderma)</li> <li>Compromised renal function including chronic, severe kidney disease (GFR &lt; 30 ml/min/1.73m2), or acute kidney injury</li> <li>Pregnancy or breast-feeding</li> <li>Subjects who have received or plan to receive neoadjuvant chemotherapy</li> <li>Sternal notch to nipple distance of &gt; 32 cm as measured in a sitting or standing position</li> <li>Measurement of widest circumference around breasts and arms &gt; 135 cm</li> <li>Known allergy to device components</li> <li>Multicentric tumors (additional tumors &gt; 2 cm from primary)</li> <li>Infectious or inflammatory processes near the area of intervention</li> <li>Planned surgery with localization devices including WGL, intraoperative ultrasound guidance, radiofrequency emitting implants, magnetic seeds, radioactive seeds, and tissue inspection devices</li> <li>Simultaneous participation in an interventional study or participation in an interventional study in the last 1 month before study inclusion</li> <li>Known drug and/or alcohol abuse</li> <li>Mental incapacity that precludes adequate understanding or cooperation</li> </ol> <p>Only for patient of center 03: 15N: If no, Is the patient participating in another interventional study?</p> |              |                                |

|  |                           |                  |                |
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**Table 8A. Medical history – General information**

**Safety Analysis Set**


|   |              | <b>SAS<br/>(N=XX)</b> |
|---|--------------|-----------------------|
| <b>Examination performed</b>                                |              |                       |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Contraindications to MRI</b>                             |              |                       |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>History of adverse event to gadolinium</b>               |              |                       |
| <b>Yes</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b> | X (XX.X)              |
| MRI: Magnetic Resonance Imaging<br>SAS: Safety Analysis Set |              |                       |

|   |                           |                  |                |
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**Table 9B. Medical history – Previous and ongoing conditions**

**Safety Analysis Set**


|  |              | <b>SAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>Infections and infestations</b>           |              |                       |
| <b>Yes</b>                                   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>                                    | <b>N (%)</b> | X (XX.X)              |
| <b>Neoplasm (including cysts and polyps)</b> |              |                       |
| <b>Yes</b>                                   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>                                    | <b>N (%)</b> | X (XX.X)              |
| <b>Variable X</b>                            |              |                       |
| <b>Yes</b>                                   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>                                    | <b>N (%)</b> | X (XX.X)              |
| SAS: Safety Analysis Set                     |              |                       |

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
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**Table 10. Previous radiological assessments**

**Safety Analysis Set**

|  |                  | <b>SAS<br/>(N=XX)</b> |
|--|------------------|-----------------------|
| <b>Mammogram available prior to enrollment?</b>  |                  |                       |
| Yes  | N (%)            | X (XX.X)              |
| No   | N (%)            | X (XX.X)              |
| Missing  | N (%)            | X (XX.X)              |
| <b>IBC/DCIS confirmed</b>  |                  |                       |
| Yes  | N (%)            | X (XX.X)              |
| No   | N (%)            | X (XX.X)              |
| Missing  | N (%)            | X (XX.X)              |
| <b>Prone MRI available prior to enrollment?</b>  |                  |                       |
| Yes  | N (%)            | X (XX.X)              |
| No   | N (%)            | X (XX.X)              |
| Missing  | N (%)            | X (XX.X)              |
| <b>Presence of satellite lesions less than or equal to 2 cm from the primary</b>               |                  |                       |
| Yes  | N (%)            | X (XX.X)              |
| No   | N (%)            | X (XX.X)              |
| Missing  | N (%)            | X (XX.X)              |
| <b>Tumor maximal diameter (cm)</b>   | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Pathological analysis of diagnostic core biopsy specimens available prior to enrollment</b> |                  |                       |
| Yes  | N (%)            | X (XX.X)              |
| No   | N (%)            | X (XX.X)              |
| Missing  | N (%)            | X (XX.X)              |
| <b>If Yes, IBC or DCIS</b>   |                  |                       |

|   |                           |                  |                |
|---|---------------------------|------------------|----------------|
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|  |              | <b>SAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>IBC</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>DCIS</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Both</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| IBC: Invasive Breast Cancer<br>DCIS: Ductal Carcinoma In Situ<br>MRI: Magnetic Resonance Imaging<br>SAS: Safety Analysis Set |              |                       |

|  |                           |                  |                |
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**Table 11. Supine MRI**

**Safety Analysis Set**


|   |                  | <b>SAS<br/>(N=XX)</b> |
|---|------------------|-----------------------|
| <b>Was supine MRI performed?</b>                            |                  |                       |
| <b>Yes</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Where images transferred to CairnSurgical?</b>           |                  |                       |
| <b>Yes</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Tumor maximal diameter (cm)</b>                          | <b>Mean ± SD</b> | XX ± X                |
|   | <b>Min - max</b> | XX - X                |
|   | <b>Missing</b>   | X                     |
| <b>Tumor volume (cm<sup>3</sup>)</b>                        | <b>Mean ± SD</b> | XX ± X                |
|   | <b>Min - max</b> | XX - X                |
|   | <b>Missing</b>   | X                     |
| <b>Optimal resection volume (cm<sup>3</sup>)</b>            | <b>Mean ± SD</b> | XX ± X                |
|   | <b>Min - max</b> | XX - X                |
|   | <b>Missing</b>   | X                     |
| MRI: Magnetic Resonance Imaging<br>SAS: Safety Analysis Set |                  |                       |

|   |                           |                  |                |
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**Table 12. Prior medications**

**Safety Analysis Set**


|   |                           |              | <b>SAS<br/>(N=XX)</b> |
|---|---------------------------|--------------|-----------------------|
| <b>Did patients take at least one prior medication?</b> |                           |              |                       |
| <b>Yes</b>  |                           | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>   |                           | <b>N (%)</b> | X (XX.X)              |
| <b>Indication A</b>                                     | <b>Active principle</b>   |              |                       |
|   | <b>Active principle A</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Active principle B</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Overall</b>            | <b>N (%)</b> | X (XX.X)              |
| <b>Indication B</b>                                     | <b>Active principle</b>   |              |                       |
|   | <b>Active principle A</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Active principle B</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Overall</b>            | <b>N (%)</b> | X (XX.X)              |
| SAS: Safety Analysis Set                                |                           |              |                       |

|  |                           |                  |                |
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**Table 13. Concomitant medications**

**Safety Analysis Set**


|   |                           |              | <b>SAS<br/>(N=XX)</b> |
|---|---------------------------|--------------|-----------------------|
| <b>Did patients take at least one concomitant medication?</b> |                           |              |                       |
| <b>Yes</b>  |                           | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>   |                           | <b>N (%)</b> | X (XX.X)              |
| <b>Indication A</b>   | <b>Active principle</b>   |              |                       |
|   | <b>Active principle A</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Active principle B</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Overall</b>            | <b>N (%)</b> | X (XX.X)              |
| <b>Indication B</b>   | <b>Active principle</b>   |              |                       |
|   | <b>Active principle A</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Active principle B</b> | <b>N (%)</b> | X (XX.X)              |
|   | <b>Overall</b>            | <b>N (%)</b> | X (XX.X)              |
| SAS: Safety Analysis Set                                      |                           |              |                       |

|  |                           |                  |                |
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**Table 14. Surgery and positive margin evaluation**

**Full Analysis Set, Per Protocol Set**


|  |              | <b>FAS<br/>(N=XX)</b> | <b>PPS<br/>(N=XX)</b> |
|--|--------------|-----------------------|-----------------------|
| <b>Surgery performed?</b>  |              |                       |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Tumor specimen removed?</b>   |              |                       |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Specimen mammogram obtained</b>   |              |                       |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Tumor specimen sent to the pathologist for evaluation of the positive margins</b> |              |                       |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Positive margins detected</b>   |              |                       |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              | X (XX.X)              |
| <b>95% Confidence Interval</b>   |              | (XX.XX – XX.XX)       | (XX.XX – XX.XX)       |
| FAS: Full Analysis Set<br>PPS: Pere Protocol Set                                     |              |                       |                       |

|  |                           |                  |                |
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**Table 15. Specimen and tumor volumes**

**Full Analysis Set**


|  |                  | <b>FAS<br/>(N=XX)</b> |
|--|------------------|-----------------------|
| <b>Supine MRI*</b>   |                  |                       |
| <b>Tumor maximal diameter (cm)</b>   | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Tumor volume (cm<sup>3</sup>)</b>   | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Optimal resection volume (cm<sup>3</sup>)</b>   | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>After Surgery at V2</b>   |                  |                       |
| <b>Specimen volume determined by water displacement (ml)</b>   | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Maximal tumor diameter on pathology report of lumpectomy specimen (cm)</b>  | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <p>*Results from Table 10. Supine MRI displayed again for comparison purposes</p> <p>MRI: Magnetic Resonance Imaging<br/>FAS: Full Analysis Set<br/>SD: Standard Deviation</p> |                  |                       |

|  |                           |                  |                |
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**Table 16. Shave biopsies**

**Full Analysis Set**


|   |                  | <b>FAS<br/>(N=XX)</b> |
|---|------------------|-----------------------|
| <b>Shave biopsies done</b>  |                  |                       |
| <b>Yes</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>   | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Number</b>   |                  |                       |
| <b>1</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>2</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>3</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>X</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Volume of shave biopsy determined<br/>by water displacement (ml)</b> | <b>Mean ± SD</b> | XX ± X                |
|   | <b>Min - max</b> | XX - X                |
|   | <b>Missing</b>   | X                     |
| SD: Standard Deviation<br>FAS: Full Analysis Set                        |                  |                       |

|  |                           |                  |                |
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**Table 17. Cancer Characteristics in Biopsy and Lumpectomy**

**Full Analysis Set**


|   |              | <b>FAS<br/>(N=XX)</b> |
|---|--------------|-----------------------|
| <b>IBC or DCIS from core biopsy *</b>   |              |                       |
| <b>IBC</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>DCIS</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Both</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>IBC or DCIS in lumpectomy specimen</b>   |              |                       |
| <b>IBC</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>DCIS</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Both</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>If invasive, subtype</b>   |              |                       |
| <b>IBC</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>DCIS</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Both</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>  | <b>N (%)</b> | X (XX.X)              |
| IBC: Invasive Breast Cancer<br>DCIS: Ductal Carcinoma In Situ<br>FAS: Full Analysis Set |              |                       |

|  |                           |                  |                |
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**Table 18. Likert questionnaire for ease of use of BCL**

**Full Analysis Set**


|  |              | <b>FAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>Likert questionnaire completed by investigator</b>  |              |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>1. Overall, how satisfied or dissatisfied are you with the BCL device?</b>  |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Neither satisfied nor dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Question X*</b>   |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Neither satisfied nor dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <p>* See the paragraph "<i>Likert Questionnaire for Ease of Use of BCL</i>" in collected variables in section 6.2.2 Analysis of Secondary Variables for the full list of items</p> <p>FAS: Full Analysis Set</p> |              |                       |

|  |                           |                  |                |
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**Table 19. Likert questionnaire the Visualizer**

**Full Analysis Set**


|  |              | <b>FAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>Likert questionnaire completed by investigator</b>  |              |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>1. Overall, how satisfied or dissatisfied are you with the Visualizer?</b>  |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Neither satisfied nor dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Question X*</b>   |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Neither satisfied nor dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <p>* See the paragraph "<i>Likert Questionnaire for Visualizer</i>" in collected variables in section 6.2.2 Analysis of Secondary Variables for the full list of items</p> <p>FAS: Full Analysis Set</p> |              |                       |

|  |                           |                  |                |
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**Table 20A. Breast-Q – Single items**

**Full Analysis Set**


|  |              | <b>FAS<br/>(N=XX)</b> |
|--|--------------|-----------------------|
| <b>Breast-Q completed by the patient</b>   |              |                       |
| <b>Yes</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>PRE-OPERATIVE MODULE</b>  |              |                       |
| <b>How you look in the mirror clothed</b>  |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Question X*</b>   |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>POST-OPERATIVE MODULE</b>   |              |                       |
| <b>Question X*</b>   |              |                       |
| <b>Very satisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow satisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Somehow dissatisfied</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Very dissatisfied</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b> | X (XX.X)              |
| <p>* See the paragraph “BREAST-Q” in collected variables in section 6.2.2 Analysis of Secondary Variables for the full list of items</p> <p>FAS: Full Analysis Set</p> |              |                       |

|   |                           |                  |                |
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**Table 21B. Breast-Q – Total scores**

**Full Analysis Set**


|                             |                  | <b>FAS<br/>(N=XX)</b> |                      |
|-----------------------------|------------------|-----------------------|----------------------|
|                             |                  | <b>PREOPERATIVE</b>   | <b>POSTOPERATIVE</b> |
| <b>BREAST-Q raw score</b>   | <b>Mean ± SD</b> | XX ± X                | XX ± X               |
|                             | <b>Min - max</b> | XX - X                | XX - X               |
|                             | <b>Missing</b>   | X                     | X                    |
| <b>BREAST-Q Rasch score</b> | <b>Mean ± SD</b> | XX ± X                | XX ± X               |
|                             | <b>Min - max</b> | XX - X                | XX - X               |
|                             | <b>Missing</b>   | X                     | X                    |
| FAS: Full Analysis Set      |                  |                       |                      |

|  |                           |                  |                |
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**Table 22A. Summary of adverse events – AE occurrence**

**Safety Analysis Set**


|   |              | <b>SAS<br/>(N=XX)</b> |
|---|--------------|-----------------------|
| <b>Number of patients with at least one AE</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Number of patients with at least one related AE</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Number of patients with at least one serious AE</b>  | <b>N (%)</b> | X (XX.X)              |
| <b>Number of patients with at least one severe AE</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Number of patients who prematurely terminated the study due to an AE</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Number of deaths</b>   | <b>N (%)</b> | X (XX.X)              |
| <b>Number of AEs</b>  | <b>N</b>     | X                     |
| <b>Number of SAEs</b>   | <b>N</b>     | X                     |
| <b>Number of related* AEs</b>   | <b>N</b>     | X                     |
| <b>Number of severe AEs</b>   | <b>N</b>     | X                     |
| <b>Number of events</b>   | <b>N</b>     | X                     |
| <p>* Includes answers: Possible, Probable or Causal relationship</p> <p>AE: Adverse Event<br/> PT: Preferred Term<br/> SAE: Serious Adverse Event<br/> SAS: Safety Analysis Set</p> |              |                       |

|  |                           |                  |                |
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**Table 23B. Summary of adverse events – MedDRA coding**

**Safety Analysis Set**

| SOC name  | PT name   |       | SAS<br>(N=XX) |
|---|-----------|-------|---------------|
| SOC name 1  | PT term 1 | N (%) | X (XX.X)      |
|   | PT term 2 | N (%) | X (XX.X)      |
|   | PT term X | N (%) | X (XX.X)      |
|   | OVERALL   | N (%) | X (XX.X)      |
| SOC name X  | PT term 1 | N (%) | X (XX.X)      |
|   | PT term 2 | N (%) | X (XX.X)      |
|   | PT term X | N (%) | X (XX.X)      |
|   | OVERALL   | N (%) | X (XX.X)      |
| SOC: System Organ Class<br>PT: Preferred Term<br>SAS: Safety Analysis Set |           |       |               |


|  |                           |                  |                |
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**Table 24. Incidence of AEs by relationship with IP**

**Safety Analysis Set**

| SOC name   | PT name   | Relationship with IP |       | SAS<br>(N=XX) |
|------------|-----------|----------------------|-------|---------------|
| SOC term X | PT term 1 | Not related          | N (%) | X (XX.X)      |
|            |           | Possible             | N (%) | X (XX.X)      |
|            |           | Probable             | N (%) | X (XX.X)      |
|            |           | Causal               | N (%) | X (XX.X)      |
|            |           | Overall              | N (%) | X (XX.X)      |
|            | PT term 2 | Not related          | N (%) | X (XX.X)      |
|            |           | Possible             | N (%) | X (XX.X)      |
|            |           | Probable             | N (%) | X (XX.X)      |
|            |           | Causal               | N (%) | X (XX.X)      |
|            |           | Overall              | N (%) | X (XX.X)      |
|            | Overall   | Not related          | N (%) | X (XX.X)      |
|            |           | Possible             | N (%) | X (XX.X)      |
|            |           | Probable             | N (%) | X (XX.X)      |
|            |           | Causal               | N (%) | X (XX.X)      |
|            |           | Overall              | N (%) | X (XX.X)      |

AE: Adverse Event  
IP: Investigational Product  
SOC: System Organ Class  
PT: Preferred Term  
SAS: Safety Analysis Set

|  |                           |                  |                |
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**Table 25. Incidence of AEs by severity**

**Safety Analysis Set**

| SOC name   | PT name   | Severity |       | SAS<br>(N=XX) |
|------------|-----------|----------|-------|---------------|
| SOC term X | PT term 1 | Mild     | N (%) | X (XX.X)      |
|            |           | Moderate | N (%) | X (XX.X)      |
|            |           | Severe*  | N (%) | X (XX.X)      |
|            |           | Overall  | N (%) | X (XX.X)      |
|            | PT term 2 | Mild     | N (%) | X (XX.X)      |
|            |           | Moderate | N (%) | X (XX.X)      |
|            |           | Severe*  | N (%) | X (XX.X)      |
|            |           | Overall  | N (%) | X (XX.X)      |
|            | Overall   | Mild     | N (%) | X (XX.X)      |
|            |           | Moderate | N (%) | X (XX.X)      |
|            |           | Severe*  | N (%) | X (XX.X)      |
|            |           | Overall  | N (%) | X (XX.X)      |

\* includes answers: Severe or medically significant, Life-threatening consequences or urgent intervention indicated, Death related to AE)

AE: Adverse Event  
SOC: System Organ Class  
PT: Preferred Term  
SAS: Safety Analysis Set


|  |                           |                  |                |
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**Table 26. Incidence of SAEs**

**Safety Analysis Set**

| SOC name   | PT name   | Seriousness |       | SAS<br>(N=XX) |
|------------|-----------|-------------|-------|---------------|
| SOC term X | PT term 1 | Not serious | N (%) | X (XX.X)      |
|            |           | Serious     | N (%) | X (XX.X)      |
|            |           | Overall     | N (%) | X (XX.X)      |
|            | PT term 2 | Not serious | N (%) | X (XX.X)      |
|            |           | Serious     | N (%) | X (XX.X)      |
|            |           | Overall     | N (%) | X (XX.X)      |
|            | Overall   | Not serious | N (%) | X (XX.X)      |
|            |           | Serious     | N (%) | X (XX.X)      |
|            |           | Overall     | N (%) | X (XX.X)      |

SAE: Serious Adverse Event  
SOC: System Organ Class  
PT: Preferred Term  
SAS: Safety Analysis Set


|  |                           |                  |                |
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**Table 27. Incidence of AEs leading to study termination**

**Safety Analysis Set**

| SOC name   | PT name   | Action taken       |       | SAS<br>(N=XX) |
|------------|-----------|--------------------|-------|---------------|
| SOC term X | PT term 1 | No action taken    | N (%) | X (XX.X)      |
|            |           | Study Discontinued | N (%) | X (XX.X)      |
|            |           | Overall            | N (%) | X (XX.X)      |
|            | PT term 2 | No action taken    | N (%) | X (XX.X)      |
|            |           | Study Discontinued | N (%) | X (XX.X)      |
|            |           | Overall            | N (%) | X (XX.X)      |
|            | Overall   | No action taken    | N (%) | X (XX.X)      |
|            |           | Study Discontinued | N (%) | X (XX.X)      |
|            |           | Overall            | N (%) | X (XX.X)      |


SOC: System Organ Class  
PT: Preferred Term  
SAS: Safety Analysis Set

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**Table 28. Incidence of deaths**

**Safety Analysis Set**


|   |              | <b>SAS<br/>(N=XX)</b> |
|---|--------------|-----------------------|
| <b>Non-fatal AE</b>                           | <b>N (%)</b> | X (XX.X)              |
| <b>Fatal AE</b>                               | <b>N (%)</b> | X (XX.X)              |
| AE: Adverse Event<br>SAS: Safety Analysis Set |              |                       |

|   |                           |                  |                |
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**Table 29. Clinical laboratory evaluation**

**Safety Analysis Set**

|  |                  | <b>SAS<br/>(N=XX)</b> |
|--|------------------|-----------------------|
| <b>Evaluation performed?</b>   |                  |                       |
| <b>Yes</b>   | <b>N (%)</b>     | X (XX.X)              |
| <b>No</b>  | <b>N (%)</b>     | X (XX.X)              |
| <b>Missing</b>   | <b>N (%)</b>     | X (XX.X)              |
| <b>Hemoglobin</b>  | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Hematocrit</b>  | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <b>Parameter X*</b>  | <b>Mean ± SD</b> | XX ± X                |
|  | <b>Min - max</b> | XX - X                |
|  | <b>Missing</b>   | X                     |
| <p>* See <i>collected variables</i> in section 6.4.2 Clinical Laboratory Evaluation for the full list of parameters</p> <p>SD: Standard Deviation<br/>SAS: Safety Analysis Set</p> |                  |                       |

|  |                           |                  |                |
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**Table 30. Vital signs**

**Safety Analysis Set**

| Visit                | Parameter  |           | SAS<br>(N=XX) |
|----------------------|--|-----------|---------------|
| Visit 0              | Evaluation performed?                                    |           |               |
|                      | Yes  | N (%)     | X (XX.X)      |
|                      | No   | N (%)     | X (XX.X)      |
|                      | Missing  | N (%)     | X (XX.X)      |
|                      | Systolic Blood Pressure                                  | Mean ± SD | XX ± X        |
|                      |  | Min - max | XX - X        |
|                      |  | Missing   | X             |
|                      | Parameter X*   | Mean ± SD | XX ± X        |
|                      |  | Min - max | XX - X        |
|                      |  | Missing   | X             |
| Visit 2 preoperative | Examination performed within 10-40 days from supine MRI? |           |               |
|                      | Yes  | N (%)     | X (XX.X)      |
|                      | No   | N (%)     | X (XX.X)      |
|                      | Missing  | N (%)     | X (XX.X)      |
|                      | Systolic Blood Pressure                                  | Mean ± SD | XX ± X        |
|                      |  | Min - max | XX - X        |
|                      |  | Missing   | X             |
|                      | Parameter X*   | Mean ± SD | XX ± X        |
|                      |  | Min - max | XX - X        |
|                      |  | Missing   | X             |

\* See *collected variables* in section 6.4.3 Vital Signs for the full list of parameters


SD: Standard Deviation  
SAS: Safety Analysis Set

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**Table 31. Physical examination results**

**Safety Analysis Set**


| Visit  | Parameter                                      |           | SAS<br>(N=XX) |
|--|--|-----------|---------------|
| Visit 0  | Weight (kg)                                    | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
|  | Height (cm)                                    | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
|  | BMI (kg/m²)                                    | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
|  | Distance from sternal notch to the nipple (cm) | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
|  | Circumference around the breast and arms (cm)  | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
| Visit X  | Parameter X                                    | Mean ± SD | XX ± X        |
|  |  | Min - max | XX - X        |
|  |  | Missing   | X             |
| SD: Standard Deviation<br>SAS: Safety Analysis Set |  |           |               |

|   |                           |                  |                |
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**Table 32. Device deficiencies**


**Safety Analysis Set**

| Visit   | Any device deficiencies occurred during IP utilization? |       | SAS (N=XX) |
|---|---|-------|------------|
| Visit X   | No  | N (%) | X (XX.X)   |
|   | Yes   | N (%) | X (XX.X)   |
|   | Missing   | N (%) | X (XX.X)   |
| IP: Investigational Product<br>SAS: Safety Analysis Set |   |       |            |

|  |                           |                  |                |
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## 9.2. Listings

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## Listing 1A. Disposition of the patients – Study participation


### All patients

| Screening number  | IC signed | Patient eligible | Surgery performed? | Study completed? | If no, reason | If other, specify | If death, specify | Inclusion in SAS | Reason of exclusion | Inclusion in FAS | Reason of exclusion | Inclusion in PPS | Reason of exclusion |
|---|-----------|------------------|--------------------|------------------|---------------|-------------------|-------------------|------------------|---------------------|------------------|---------------------|------------------|---------------------|
| 01-001  | X         | X                |                    | X                |               |                   |                   | X                |                     | X                |                     | X                |                     |
| XX-XXX  |           | X                |                    | X                | XXXXXX        |                   |                   | X                | XXXX                | X                | XXXX                | X                | XXXX                |
| IC: Informed Consent<br>FAS: Full Analysis Set<br>PPS: Per Protocol Set<br>SAS: Safety Analysis Set |           |                  |                    |                  |               |                   |                   |                  |                     |                  |                     |                  |                     |

## Listing 2B. Disposition of the patients – Study dates

### All patients


| Screening number                          | IC date   | Screening V0 | V1        | Surgery V2 | Follow-up V3 | EOS V4    | Date of study termination |
|---|-----------|--------------|-----------|------------|--------------|-----------|---------------------------|
| 01-001                                    | XXAAAXXXX | XXAAAXXXX    | XXAAAXXXX | XXAAAXXXX  | XXAAAXXXX    | XXAAAXXXX | XXAAAXXXX                 |
| XX-XXX                                    | XXAAAXXXX | XXAAAXXXX    | XXAAAXXXX | XXAAAXXXX  | XXAAAXXXX    | XXAAAXXXX | XXAAAXXXX                 |
| IC: Informed Consent<br>EOS: End Of Study |           |              |           |            |              |           |                           |

|   |                           |                  |                |
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### Listing 3. Baseline and demographic characteristics

#### Safety Analysis Set


| Screening number | Age (years) | Ethnic group | If Other, specify | Smoking habit | Alcohol abuse | Pregnancy test performed | If no, reason | If other, specify | Pregnancy test result | Pregnancy test date |
|------------------|-------------|--------------|-------------------|---------------|---------------|--------------------------|---------------|-------------------|-----------------------|---------------------|
| 01-001           | 23          | Caucasian    |                   | Smoker        | XXX           | Yes                      |               |                   | Negative              | XXAAAXXXX           |
| 01-002           | 41          | Caucasian    |                   | Former smoker |               | NA/Male                  |               |                   |                       |                     |

|   |                           |                  |                |
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#### Listing 4. ICF protocol violations

##### All patients


| Screening number           | Details of ICF deviation | Deviation category | Deviation type |
|----------------------------|--------------------------|--------------------|----------------|
| 01-001                     | XXXXX                    | XXXXX              | XXXXX          |
| XX-XXX                     | XXXXX                    | XXXXX              | XXXXX          |
| ICF: Informed Consent Form |                          |                    |                |

|   |                           |                  |                |
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## Listing 5. Inclusion and exclusion criteria

### All patients

| Screening number   | Inclusion criteria not met | Exclusion criteria met |
|--|----------------------------|------------------------|
| 01-001   | XX , XX                    | XX                     |
| XX-XXX   |                            | XX , XX                |
| <p>Inclusion criteria:</p> <ol style="list-style-type: none"> <li>1. Patient Informed consent form (ICF) signed</li> <li>2. Female Aged = 18 years at the time of the signature of ICF</li> <li>3. Histologic diagnosis of IBC or DCIS</li> <li>4. Tumor excision that will require localization because it cannot be definitively defined by palpation</li> <li>5. The tumor is unifocal; possible satellite lesions &lt; 2 cm from primary are eligible</li> <li>6. The tumor enhances and is greater than or equal to 5mm on prone breast MRI imaging</li> <li>7. Subject and surgeon agree to perform BCS</li> <li>8. Willingness to follow all study procedures, including attending all site visits, tests and examinations</li> </ol> <p>Exclusion criteria</p> <ol style="list-style-type: none"> <li>1. Severe claustrophobia</li> <li>2. Contraindication to use of gadolinium-based intravenous contrast, including life-threatening allergy</li> <li>3. Uncontrolled cardiac, renal, or pulmonary disease</li> <li>4. Uncontrolled systemic disease (e.g., lupus erythematosus or scleroderma)</li> <li>5. Compromised renal function including chronic, severe kidney disease (GFR &lt; 30 ml/min/1.73m2), or acute kidney injury</li> <li>6. Pregnancy or breast-feeding</li> <li>7. Subjects who have received or plan to receive neoadjuvant chemotherapy</li> <li>8. Sternal notch to nipple distance of &gt; 32 cm as measured in a sitting or standing position</li> <li>9. Measurement of widest circumference around breasts and arms &gt; 135 cm</li> <li>10. Known allergy to device components</li> <li>11. Multicentric tumors (additional tumors &gt; 2 cm from primary)</li> <li>12. Infectious or inflammatory processes near the area of intervention</li> <li>13. Planned surgery with localization devices including WGL, intraoperative ultrasound guidance, radiofrequency emitting implants, magnetic seeds, radioactive seeds, and tissue inspection devices</li> <li>14. Simultaneous participation in an interventional study or participation in an interventional study in the last 1 month before study inclusion</li> <li>Only for patient of center 3: 15N: If no, Is the patient participating in another interventional study?</li> <li>15. Known drug and/or alcohol abuse</li> <li>16. Mental incapacity that precludes adequate understanding or cooperation</li> </ol> |                            |                        |

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## Listing 6A. Medical history – General information


### Safety Analysis Set

| Screening number | Examination performed | If no, reason | Bra cup size | Contraindications to MRI? | If yes, details | History of adverse events to gadolinium? | If yes, details |
|------------------|-----------------------|---------------|--------------|---------------------------|-----------------|--|-----------------|
| 01-001           | Yes                   |               | XXXX         | Yes                       | XXXX            | No                                       |                 |
| XX-XXX           | No                    | XXXX          |              |                           |                 |  |                 |

## Listing 7B. Medical history – Previous and ongoing conditions

### Safety Analysis Set


| Screening number | Record per subject | Type of medical issue       | Specification | Start date | End date  | Ongoing status |
|------------------|--------------------|-----------------------------|---------------|------------|-----------|----------------|
| 01-001           | 1                  | 3. Cardiovascular disorders | XXXX          | XXAAAXXXX  |           | Yes            |
| XX-XXX           | 2                  | 7. Nervous system disorders | XXXX          | XXAAAXXXX  |           | Yes            |
| XX-XXX           | 1                  | X. Condition X              | XXXX          | XXAAAXXXX  | XXAAAXXXX | No             |

|   |                           |                  |                |
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## Listing 8. Previous radiological assessments

### Safety Analysis Set


| Screening number   | Mammogram available prior to enrollment | If no, reason | IBC/DCIS confirmed | Prone MRI available prior to enrollment | If no, reason | Tumor maximal diameter (cm) | Presence of satellite lesions less than or equal to 2 cm from the primary? | pathological analysis of diagnostic core biopsy specimens available prior to enrollment | If no, reason | If Yes, IBC or DCIS |
|--|---|---------------|--------------------|---|---------------|-----------------------------|--|---|---------------|---------------------|
| 01-001   | Yes                                     |               | XXXX               | Yes                                     |               | XX.XX                       | XX   | Yes   |               | XXX                 |
| XX-XXX   | No                                      | XXXXXX        |                    | No                                      | XXXXXX        |                             | XX   | Yes   |               | XXX                 |
| IBC: Invasive Breast Cancer<br>DCIS: Ductal Carcinoma In Situ<br>MRI: Magnetic Resonance Imaging |   |               |                    |   |               |                             |  |   |               |                     |

|   |                           |                  |                |
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## Listing 9. Supine MRI

### Safety Analysis Set


| Screening number                | Was supine MRI performed | If no, reason | Tumor maximal diameter (cm) | Tumor volume (cm <sup>3</sup> ) | Optimal resection volume (cm <sup>3</sup> ) | Images transferred to CairnSurgical | If no, reason |
|---------------------------------|--------------------------|---------------|-----------------------------|---------------------------------|---|-------------------------------------|---------------|
| 01-001                          | Yes                      |               | XX.XX                       | XX.XX                           | XX.XX                                       | Yes                                 |               |
| XX-XXX                          | No                       | XXXXXX        |                             |                                 |   | No                                  | XXXXXX        |
| MRI: Magnetic Resonance Imaging |                          |               |                             |                                 |   |                                     |               |

|   |                           |                  |                |
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## Listing 10. Prior and concomitant medications

### All patients


| Screening number  | Medication | Active principle | AE reference number | Indication | Dose-unit | Frequency | Administration form | Route of administration | Start date | End date | Ongoing status | Prior or Concomitant |
|-------------------|------------|------------------|---------------------|------------|-----------|-----------|---------------------|-------------------------|------------|----------|----------------|----------------------|
| 01-001            | XXX        | XXX              | 1                   | XXX        | XXX       | XXX       | XXX                 | XXX                     | XXAAAXXX   |          | Yes            | Concomitant          |
| XX-XXX            | XXX        | XXX              | X                   | XXX        | XXX       | XXX       | XXX                 | XXX                     | XXAAAXXX   | XXAAAXXX | No             | Prior                |
| AE: adverse Event |            |                  |                     |            |           |           |                     |                         |            |          |                |                      |

|   |                           |                  |                |
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## Listing 11. Surgery and positive margin evaluation

### Full Analysis Set


| Screening number | Was surgery performed? | If no, reason | Date of surgery | Was Tumor specimen removed? | If no, reason | Was specimen mammogram obtained? | If no, reason | Was tumor specimen sent to the pathologist for evaluation of the positive margins? | If no, reason | Were positive margins detected? |
|------------------|------------------------|---------------|-----------------|-----------------------------|---------------|----------------------------------|---------------|--|---------------|---------------------------------|
| 01-001           | Yes                    |               | XXAAAXXXX       | X                           |               | X                                |               | X  |               | X                               |
| XX-XXX           | Yes                    |               | XXAAAXXXX       | X                           | XXX           | X                                |               |  |               |                                 |

|   |                           |                  |                |
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## Listing 12. Specimen and tumor volumes

### Full Analysis Set


| Screening number  | Tumor maximal diameter from supine MRI (cm) * | Tumor volume from supine MRI (cm <sup>3</sup> ) * | Optimal resection volume from supine MRI (cm <sup>3</sup> ) * | Specimen volume determined by water displacement (ml) | Maximal tumor diameter on pathology report of lumpectomy specimen (cm) |
|---|---|---|---|---|--|
| 01-001  | XX.XX   | XX.XX   | XX.XX   | XX.XX   | XX.XX  |
| XX-XXX  | XX.XX   | XX.XX   | XX.XX   | XX.XX   | XX.XX  |
| <p>*Results from Listing 7. Supine MRI displayed again for comparison purposes</p> <p>MRI: Magnetic Resonance Imaging</p> |   |   |   |   |  |

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### Listing 13. Shave biopsies

#### Full Analysis Set


| Screening number | Shave biopsies done? | If Yes, how many? | Volume of shave biopsy determined by water displacement (ml) |
|------------------|----------------------|-------------------|--|
| 01-001           | XX                   | XX                | XX   |
| XX-XXX           | XX                   | XX                | XX   |

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## Listing 14. Cancer Characteristics in Biopsy and Lumpectomy

### Full Analysis Set


| Screening number  | IBC or DCIS from core biopsy * | IBC or DCIS in lumpectomy specimen | If invasive, subtype | If other, please specify |
|---|--------------------------------|------------------------------------|----------------------|--------------------------|
| 01-001  | XX                             | XX                                 | XX                   |                          |
| XX-XXX  | XX                             | XX                                 | XX                   | XXXXX                    |
| <p>*Results from Listing 6. Previous Radiological assessments displayed again for comparison purposes</p> <p>IBC: Invasive Breast Cancer<br/>DCIS: Ductal Carcinoma In Situ</p> |                                |                                    |                      |                          |

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## Listing 15. Likert questionnaire for ease of use of BCL

### Full Analysis Set


| Screening number | Likert questionnaire completed by investigator | If no, reason | 1. Overall, how satisfied or dissatisfied are you with the BCL device? | 2. How would you rate the ease of use of the BCL device? | 3. How much, in your opinion, has the BCL device simplified surgery? | 4. How much, in your opinion, did the BCL device speed up surgery? | 5. How would you rate the safety of the BCL device? | 6. How would you rate the reliability of the BCL device? | 7. How likely would you be to reuse the BCL device? | 8. How likely would you be to recommend the use of the BCL device to your colleagues? |
|------------------|--|---------------|--|--|--|--|---|--|---|---|
| 01-001           | Yes  |               | X  | X  | X  | X  | X   | X  | X   | X   |
| XX-XXX           | No   | XXX           |  |  |  |  |   |  |   |   |

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## Listing 16. Likert Questionnaire for the Visualizer

### Full Analysis Set

| Screening number | Likert questionnaire completed by investigator | If no, reason | 1. Overall, how satisfied or dissatisfied are you with the Visualizer? | 2. How would you rate the clarity of the 3D tumor image created by the Visualizer? | 3. How would you rate the reliability of the 3D tumor image created by the Visualizer? | 4. How would you rate the ease of use of the Visualizer? | 5. How much, in your opinion, did the Visualizer help surgery? | 6. How much, in your opinion, did the Visualizer speed up surgery? | 7. How likely would you be to reuse the Visualizer? | 8. How likely would you be to recommend the use of the Visualizer to your colleagues? |
|------------------|--|---------------|--|--|--|--|--|--|---|---|
| 01-001           | Yes  |               | X  | X  | X  | X  | X  | X  | X   | X   |
| XX-XXX           | No   | XXX           |  |  |  |  |  |  |   |   |

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### Listing 17A. Breast-Q – pre-operative module


#### Full Analysis Set

| Screening number | BREAST-Q questionnaire completed by the patient | If no, reason | A. How you look in the mirror clothed? | B. How comfortably do your bras fit? | C. Being able to wear clothing that is more fitted? | D. How you look in the mirror unclothed? | Pre-operative raw score | Pre-operative Rasch score |
|------------------|---|---------------|--|--------------------------------------|---|--|-------------------------|---------------------------|
| 01-001           | Yes   |               | X                                      | X                                    | X   | X  | XX                      | XX                        |
| XX-XXX           | No  | XXX           |  |                                      |   |  |                         |                           |

### Listing 18B. Breast-Q – post-operative module

#### Full Analysis Set


| Screening number | A. How you look in the mirror clothed? | B. The shape of your lumpectomy breast when you are wearing a bra? | C. How normal you feel in your clothes? | D. Being able to wear clothing that is more fitted? | E. How your lumpectomy breast sits/hangs? | F. How smoothly shaped your lumpectomy breast looks? | G. The contour (outline) of your lumpectomy breast? | H. How equal in size your breasts are to each other? | I. How normal your lumpectomy breast looks? | J. How much your breasts look the same? | K. How you look in the mirror unclothed? | Pre-operative raw score | Pre-operative Rasch score |
|------------------|--|--|---|---|---|--|---|--|---|---|--|-------------------------|---------------------------|
| 01-001           | X                                      | X  | X                                       | X   | X   | X  | X   | X  | X   | X                                       | X  | XX                      | XX                        |
| XX-XXX           | X                                      | X  | X                                       | X   | X   | X  | X   | X  | X   | X                                       | X  | XX                      | XX                        |

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## Listing 19. Adverse events

### Safety Analysis Set


| Screening number   | AE reference number | AE description | PT  | LLT | SOC | Outcome | Severity | Treatment | Relationship | Action taken | Seriousness | Start date | End date  | Ongoing status |
|--|---------------------|----------------|-----|-----|-----|---------|----------|-----------|--------------|--------------|-------------|------------|-----------|----------------|
| 01-001   | X                   | XXX            | XXX | XXX | XXX | XXX     | XXX      | XXX       | XXX          | XXX          | XXX         | XXAAAXXXX  | XXAAAXXXX | No             |
| XX-XXX   | X                   | XXX            | XXX | XXX | XXX | XXX     | XXX      | XXX       | XXX          | XXX          | XXX         | XXAAAXXXX  | XXAAAXXXX | No             |
| AE: Adverse Event<br>PT: Preferred Term<br>LLT: Lowest Level Term<br>SOC: System Organ Class |                     |                |     |     |     |         |          |           |              |              |             |            |           |                |

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## Listing 20. Clinical laboratory evaluation results

### Safety Analysis Set


| Screening number | Was blood sample collected? | If no, reason | Blood sample collection date | Parameter  | Parameter evaluated? | Value | Out of range? | Lower limit of Normal Range | Upper limit of Normal Range |
|------------------|-----------------------------|---------------|------------------------------|------------|----------------------|-------|---------------|-----------------------------|-----------------------------|
| 01-001           | Yes                         |               | XXAAAYYYY                    | Hemoglobin | Yes                  | XX.XX | No            | XX.X                        | XX.X                        |
| 01-001           | Yes                         |               | XXAAAYYYY                    | Hematocrit | Yes                  | XX.XX | No            | XX.X                        | XX.X                        |
| XX-XXX           | No                          | XXX           |                              |            |                      |       |               |                             |                             |

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## Listing 21. Vital signs

### Safety Analysis Set


| Screening number | Study visit | Pre or post-surgery | Examination performed within 10-40 days from supine MRI/ after discharge | If no, reason | Examination performed | If no, reason | Systolic Blood Pressure (mmHg) | Diastolic Blood Pressure (mmHg) | Heart rate (beats/min) | O <sub>2</sub> saturation (%) |
|------------------|-------------|---------------------|--|---------------|-----------------------|---------------|--------------------------------|---------------------------------|------------------------|-------------------------------|
| 01-001           | Visit 1     |                     |  |               | Yes                   |               | XX                             | XX                              | XX                     | XX                            |
| XX-XXX           | Visit 2     | Pre                 | Yes  |               |                       |               | XX                             | XX                              | XX                     | XX                            |
| XX-XXX           | Visit 2     | Post                | Yes  |               |                       |               |                                |                                 |                        |                               |
| XX-XXX           | Visit X     |                     |  |               | No                    | XXXX          |                                |                                 |                        |                               |

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## Listing 22. Physical examination results

### Safety Analysis Set


| Screening number | Study visit | Physical examination performed | If no, reason | Weight (kg) | Height (cm) | BMI (kg/m <sup>2</sup> ) | Distance from sternal notch to the nipple (cm) | Circumference around the breast and arms (cm) | Specific documentation that the breast cancer cannot be palpated | Other abnormalities, if any |
|------------------|-------------|--------------------------------|---------------|-------------|-------------|--------------------------|--|---|--|-----------------------------|
| 01-001           | Visit 0     | Yes                            |               | XX.XX       | XX.XX       | XX.XX                    | XX.XX  | XX.XX   | XXXXX  | XXXXX                       |
| XX-XXX           | Visit X     | No                             | XXXXX         |             |             |                          |  |   |  |                             |

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## Listing 23. Device Deficiencies


### Safety Analysis Set

| Screening number            | Visit   | Any device deficiencies occurred during IP utilization? |
|-----------------------------|---------|---|
| 01-001                      | Visit X | Yes   |
| XX-XXX                      | Visit X | No  |
| IP: Investigational Product |         |   |

|   |                           |                  |                |
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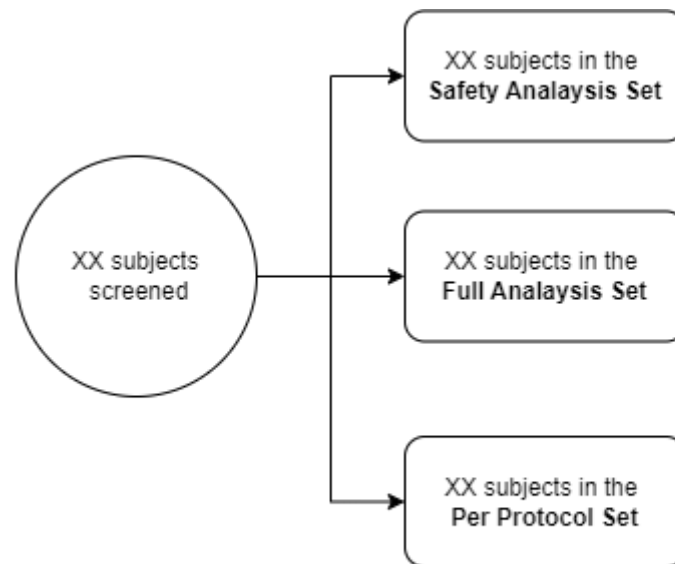
### 9.3. Figures


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**Figure 1. Disposition of the patients**

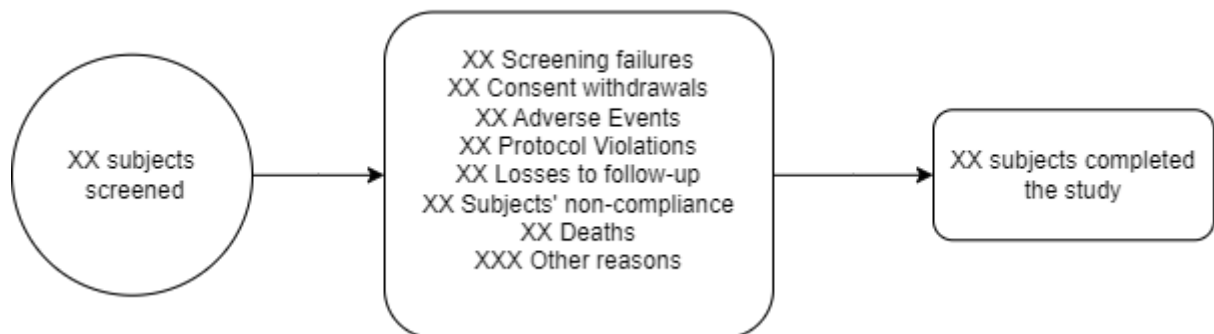
**All patients**




|   |                           |                  |                |
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**Figure 2. Status of study termination**

**All patients**



|   |                           |                  |                |
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**Figure 3. Positive margins**

**Full Analysis Set, Per Protocol Set**

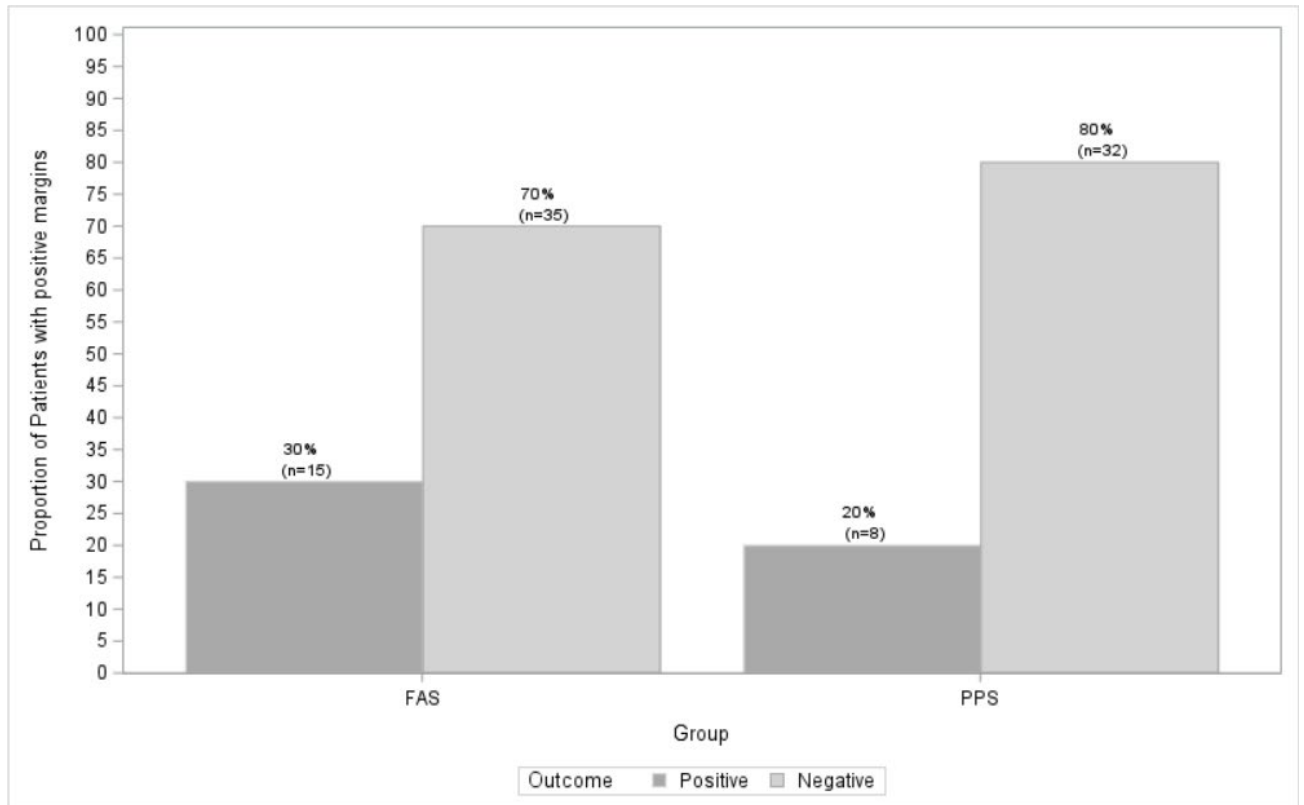
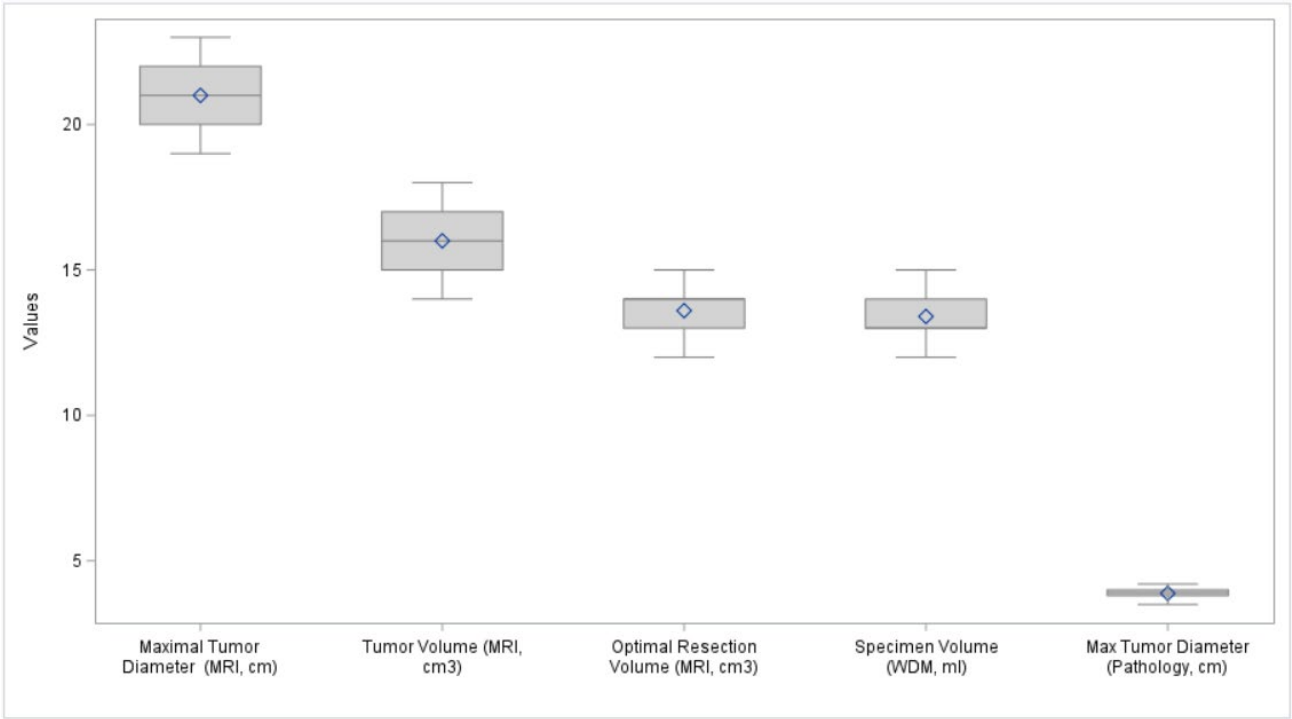



Figure 4. Tumor and specimen volumes

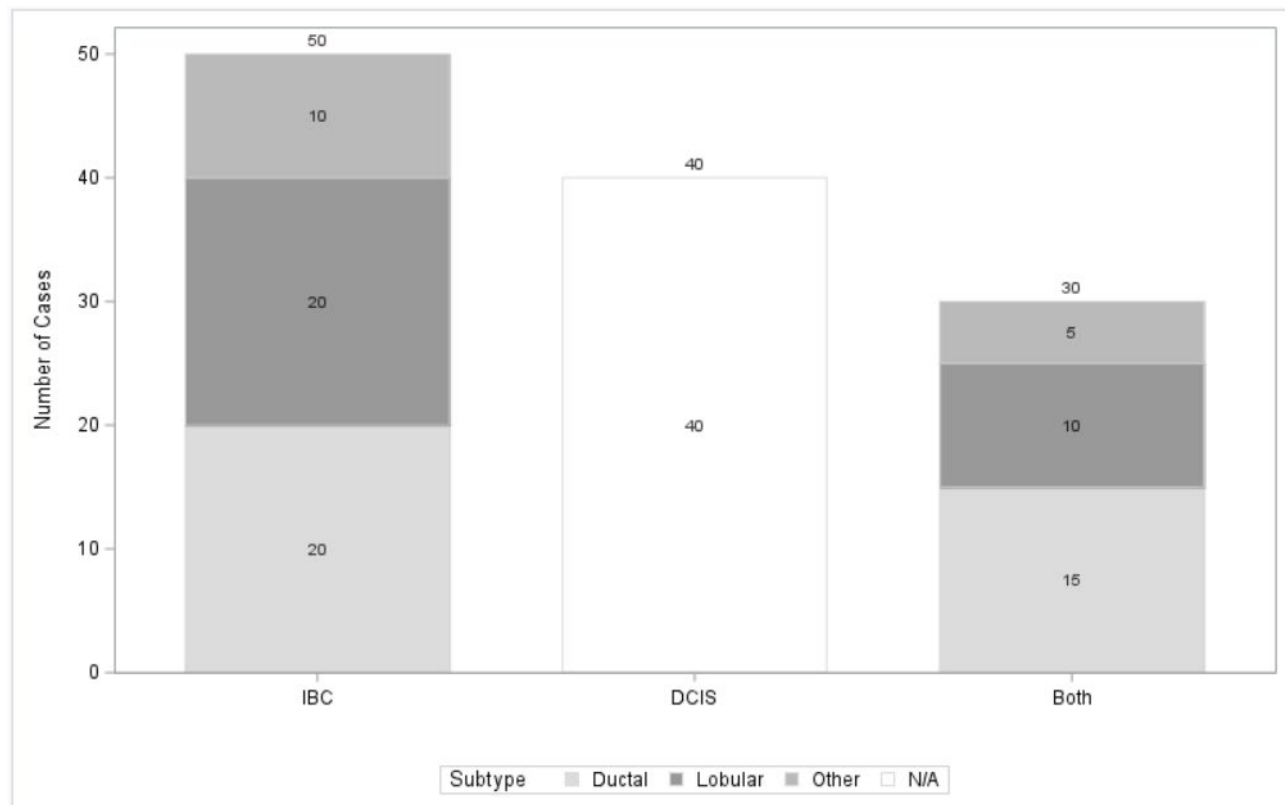
Full Analysis Set




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**Figure 5. Tumor classification**

**Full Analysis Set**



|  |                           |                  |                |
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**Figure 6. BREAST-Q scores**

**Full Analysis Set**

