

Pre- versus sub-pectoral implant-based breast reconstruction after nipple-sparing mastectomy (OPBC-02 PREPEC): A pragmatic, multicenter, randomized, superiority trial

According to the Swiss Certified Breast Center Database, 1580 implant-based breast reconstructions (IBBR) were performed at Swiss certified breast cancer centers in 2017. The optimal positioning of the breast implant above (pre-pectoral) or below the pectoralis major muscle (sub-pectoral) is currently not clear when performing IBBR after nipple-sparing mastectomy (NSM) for breast cancer treatment or prevention. Pre-pectoral positioning respects the anatomic position of the mammary gland and avoids surgery-induced alterations of the pectoralis major muscle. Therefore, it offers a variety of potential advantages including improved physical well-being, easier recovery, and aesthetically, no visible animation deformity caused by muscle movement. However, the lack of muscle coverage may create its own set of problems, including a higher risk of complications, capsular contracture and rippling of the implant.

Sub-pectoral IBBR is still standard care in many countries, but pre-pectoral IBBR is increasingly performed. However, despite this change in practice, there is no clear evidence to support the assumption that pre-pectoral positioning offers relevant improvements in patient-relevant outcomes after surgery in the long term. The Oncoplastic Breast Consortium (OPBC) consensus conference was held in Basel in March 2018 and involved 44 specialized oncologic, oncoplastic and reconstructive breast surgeons from 14 countries across four continents. One of the main conclusions, which we address by the present proposal, was that the heterogeneity in breast reconstruction practice calls for RCTs to guide treatment decisions.

We hypothesize that pre-pectoral IBBR is associated with improved quality of life compared to sub-pectoral IBBR by improving long-term physical well-being (chest). We propose a pragmatic, multicenter, randomized, parallel-group, superiority trial of 24 months follow-up to test this hypothesis. We designed the trial to be fit for that purpose by applying the PRECIS-2 requirements for pragmatism. The trial will include 372 patients undergoing NSM and IBBR for prevention or treatment of breast cancer at 13 Swiss and 3 European OPBC study sites, of which four are private centers and five are University hospitals. Exclusion criteria are in accordance with the patient population in usual care. Randomization will be stratified by center and uni- versus bilateral surgery and performed using the web-based clinical data management system secuTrial. Patients will be randomized 1:1 to the experimental group with pre-pectoral IBBR and the control group with sub-pectoral IBBR following a standard minimization procedure. Patient advocates have helped develop the protocol and select the primary endpoint, which will be patient-reported long-term physical well-being (chest) measured by the BREAST-Q scale “physical well-being: chest” at 24 months after NSM and immediate breast reconstruction. Secondary endpoints will include safety, overall quality of life, patient satisfaction, objective aesthetic outcomes and burden on patients. Outcome assessment of all secondary endpoints will be masked to group assignment. Primary analysis will be intention-to-treat. The study duration will be four years.

We believe that this trial is original and relevant inasmuch as it addresses a specific clinical research field that is important and under-investigated, and feasible for the following reasons: First, the corresponding applicant is an oncoplastic surgeon with experience in performing multicenter randomized trials. Second, he developed this proposal with the help of his co-applicant, a reconstructive breast surgeon specialized in breast reconstruction, and a team of patient advocates and experienced clinical research partners from all relevant disciplines. Third, a strong network of recruiting centers from public and private settings that has proved to operate well together in the past will ensure sufficient patient accrual.