BILATERAL PROPHYLACTIC MASTECTOMY AND IMMEDIATE BREAST RECONSTRUCTION WITH IMPLANTS

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BILATERAL PROPHYLACTIC MASTECTOMY
AND IMMEDIATE BREAST RECONSTRUCTION
WITH IMPLANTS

Jessica Gahm

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To the memory of Göran Jurell
ABSTRACT

Bilateral prophylactic mastectomy (BPM) followed by immediate breast reconstruction (IBR) has been more frequently performed over the last 10 years to prevent breast cancer in high-risk women. Since this procedure is prophylactic, it is very important to provide detailed information regarding possible consequences of surgery. The overall aim of this thesis was to increase our knowledge of outcomes after bilateral prophylactic mastectomy and immediate breast reconstruction with implants in women with increased inherited risk of breast cancer. The women were operated on between 1993- and 2001 and 2004- and 2006 at Karolinska University Hospital in Stockholm, Sweden. Follow-up time was a minimum of two years after surgery.

Breast sensitivity was assessed quantitatively and qualitatively and was found to be significantly impaired in all respects compared to a control group of non-operated women. The prevalence of pain and/or discomfort in the breasts was high (69%), but no patient reported severe pain. With regards to impact of the BPM on patients’ sexuality, a majority reported lost or substantially impaired ability to experience sexual sensations in the reconstructed breasts. Sexual enjoyment was negatively affected in 75% of the women, particularly in those who rated their breasts as very important to their sexuality prior to BPM. Despite the negative effects in sensitivity and sexuality, feelings of regret were almost non-existent, as measured with the Decision Regret Scale. Health-related quality of life was measured with the short form-36 (SF-36) questionnaire, and no difference was seen in patients vs. a reference group of Swedish women.

Corrective procedures were performed in the majority of patients which is important to inform women ahead of BPM. No patient had a severe surgical complication. The aesthetic results were evaluated both objectively and subjectively. Breast symmetry was good and equivalent to non-operated women. Patients were satisfied with the overall aesthetic outcome, but not with nipple-areola-complex reconstruction. Aesthetic outcomes of BPM and IBR with anatomically-shaped vs. round implants were not significantly different.

In conclusion, BPM and IBR with implants is a safe procedure with good aesthetic results and high patient satisfaction for the majority of patients. It should be noted that a majority of patients will lose the capacity for sexual sensation and will experience impaired sensitivity and slight pain and discomfort in the reconstructed breasts for a long time after surgery.
LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals as indicated below:

I. Jessica Gahm, Göran Jurell, Marie Wickman, Per Hansson.
   
   Sensitivity after bilateral prophylactic mastectomy and immediate reconstruction
   Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery
   42: 178-183, 2007

II. Jessica Gahm, Marie Wickman, Yvonne Brandberg
   
   Pain and discomfort in the breasts two years after bilateral prophylactic mastectomy in women with inherited risk of breast cancer - prevalence and impact on sexuality, quality of life and feelings of regret
   Submitted August the 24th 2009 to The Breast

III. Jessica Gahm, Göran Jurell, Åsa Edsander-Nord, Marie Wickman.
   
   Patient satisfaction with aesthetic outcome after bilateral prophylactic mastectomy and immediate reconstruction with implants

IV. Jessica Gahm, Åsa Edsander-Nord, Göran Jurell, Marie Wickman.
   
   Aesthetic outcome and patient satisfaction of anatomical vs. round shaped expandable implants in bilateral breast reconstruction: a randomized study.
   Submitted October 12th 2009 to Plastic and Reconstructive Surgery
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<td>ATM</td>
<td>Ataxia Telangiectasia Mutated gene</td>
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<td>BPM</td>
<td>Bilateral Prophylactic Mastectomy</td>
</tr>
<tr>
<td>BPSO</td>
<td>Bilateral Prophylactic Salpingo-oophorectomy</td>
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<td>BRCA1</td>
<td>Breast Cancer susceptibility gene 1</td>
</tr>
<tr>
<td>BRCA2</td>
<td>Breast Cancer susceptibility gene 2</td>
</tr>
<tr>
<td>CA-125</td>
<td>Cancer Antigen 125</td>
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<tr>
<td>CHEK2</td>
<td>CHK2 checkpoint homolog gene</td>
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<td>DIEP</td>
<td>Deep Inferior Epigastric Perforator</td>
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<td>DNA</td>
<td>Deoxyribonucleid acid</td>
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<td>IBR</td>
<td>Immediate Breast Reconstruction</td>
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<td>LD</td>
<td>Latissimus Dorsi muscle</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>MSA</td>
<td>Modular Sensory Analyser</td>
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<tr>
<td>NAC</td>
<td>Nipple Areola Complex</td>
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<td>PTEN</td>
<td>Phosphatase and tensin homologue gene</td>
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<td>p53</td>
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<td>SGAP</td>
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<td>STK11</td>
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<tr>
<td>TMG</td>
<td>Transverse Musculocutaneous Gracilis</td>
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<tr>
<td>TRAM</td>
<td>Transverse Rectus Abdominis Muscle</td>
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INTRODUCTION

Breast cancer is the most common malignancy in Swedish women with an incidence of approximately 7000 new cases each year. Breast cancer accounts for 25% of all new cancer cases in Swedish women per year. All cancer, including breast cancer, results from multiple gene mutations. Usually these mutations occur during life but occasionally an initial mutation that increases the risk of breast cancer is inherited from the parents. In families with several breast or ovarian cancer cases, a predisposing inherited mutation should be suspected. Increased knowledge about the familial patterns associated with high breast cancer risk, together with improved genetic profiling and breast reconstruction techniques, have resulted in significantly increased demand for bilateral prophylactic mastectomy (BPM) followed by immediate breast reconstruction (IBR) over the last 10 years; thus, the procedure warrants careful evaluation of outcomes in terms of aesthetics, complications and patient satisfaction. Since this surgical procedure is prophylactic and thus not mandatory, it is important to provide detailed information about the possible consequences and outcomes of surgery. The importance of the surgical outcome may differ for a healthy young woman who has opted for a prophylactic operation, compared to a woman with breast cancer who undergoes therapeutic mastectomy and IBR, and it has been shown that preoperative information must be improved in order to permit both informed decisions and realistic aesthetic and functional expectations for patients considering a BPM and IBR [1, 2]. Increased knowledge about the outcome of BPM with immediate breast reconstruction is therefore needed [3].

SPORADIC BREAST CANCER

Sporadic breast cancers are caused by mutations that have occurred during the person’s lifetime (after conception). Several risk-factors for such mutations have been identified. It is well-known that exposure to reproductive hormones, including those used in hormone replacement therapy and oral contraceptives, increases the risk of breast cancer. Other risk-factors include chest radiation during childhood or adolescence, increasing age, overweight and excessive use of alcohol [4-6]
INHERITED BREAST CANCER

Inherited (familial) breast cancers are characterized by an early age of disease onset and multiple breast and/or ovarian cancer cases in the family and inherited gene mutations play a role in about 25% of all cases of breast cancer [7, 8]. About 5-10% of the inherited mutations are associated with a family history pattern of autosomal dominant disease and indicate high risk for breast cancer. Those mutations are termed high-penetrance mutations and have been estimated to account for about 25% of the inherited (familial)breast cancer cases [9]. BRCA1 [10] and BRCA2 [11] are two genes containing high-penetrance mutations and were identified in 1994 and 1995. The BRCA1 and BRCA2 genes are supposed to be tumor suppressor genes and are believed to participate in DNA repair. Carriers of BRCA1 or BRCA2 mutations have an estimated lifetime risk of 50- 85% for breast cancer and 25-55 % for ovarian cancer [12-17]. Other high-penetrance mutations that increase the risk of breast cancer have also been identified in the; ATM, p53, PTEN and STK11 genes [18-20].However, these mutations are rare, and it is believed that the majority of the high-penetrance mutations responsible for breast cancer have yet to be identified. Inherited mutations associated with less prominent family patterns and smaller increases in risk of breast cancer are called low-penetrance mutations. Several low-penetrance gene mutations have been identified, of which CHEK2 is one of the most well known [21]. A single low-penetrance mutation is associated with a small increase in breast cancer risk. Lastly, environmental and lifestyle factors can act in concert with genetic factors to modify inherited breast cancer risk [22-24].
GENETIC COUNSELING

Members of families in whom an inherited mutation is suspected can be offered genetic counseling and screening for mutations in BRCA1 or BRCA2.

Members of families with a known mutation can be offered a mutation carrier test.

Genetic counseling and genetic screening or testing is considered in patients with:

- Early onset of breast/ovarian cancer (< 40 years of age)
- Breast and ovarian cancer in the same individual
- Two or more breast or ovarian cancer cases in blood relatives, not too late onset
- Presence of male breast cancer in individuals or in blood relatives
- Known BRCA1 or BRCA2 mutation in blood relatives

In general, the estimated risk of developing breast cancer is for a Swedish woman approximately 10% [25]. Preventive surgery and surveillance programs can be offered if counseling reveals a familial pattern that implies an increased risk of breast cancer, or if genetic screening shows carrier status for the BRCA1/BRC2 mutations.

Genetic counseling and screening that confirm a high breast cancer risk may set off negative psychological reactions due to increased anxiety about developing the disease. Stress over major medical decisions about prevention and severe anxiety during surveillance may occur, and some patients experience feelings of guilt about the risk of passing a genetic mutation on to their children. Family relationships may be strained if some relatives do not want to know that a genetic mutation has been detected within the family.

A negative screening result does not guarantee a normal breast cancer risk, since screening does not cover unidentified mutations. For women from families with a known mutation, a negative carrier test for BRCA1/BRC2 can provide relief from the substantial worries about developing breast cancer or passing a genetic mutation on to their children. A negative carrier test result may sometimes cause feelings of “survivor-guilt”, especially if other family members carry the mutation and face an increased cancer risk.

The benefit of a genetic screen that confirms a mutation is that preventive options can be taken. For any given patient, estimating her individual risk for breast cancer should be weighed against the possible benefits, negative effects, risks of surveillance vs. prophylactic surgery, and the patient’s personal wishes. Predictive genetic testing is a multi-step process, with pre- and post-test counseling, follow-up for preventive
strategies, and psychological support. A multidisciplinary team is recommended to manage the many varied aspects of genetic testing for these women and their families [26].

**BRCA 1**

nonsense mutation
change a G to an A
in post 5563

---

**A pedigree is a type of “family tree” that shows the cancer events that have occurred in a family. In human pedigrees, squares represent males and circles represent females. A horizontal line between a square and a circle represents a union. A vertical line issuing from the horizontal line denotes the offspring of that union. If there are more than one offspring, they are joined by a horizontal line. Each line of symbols is a generation line.**

**This pedigree traces hereditary breast and ovarian cancer in a large family with a known BRCA1 mutation. Black circles or squares signify that the person has cancer; if an additional line transectsthe symbol, then the person is dead. The age given underneath the symbol represents the age at diagnosis. br =breast cancer, ov= ovarian cancer. Yellow color= known carriers of the BRCA1 mutation. Number inside a symbol represents the birth year for that individual.**
OPTIONS FOR WOMEN AT HIGH RISK FOR BREAST CANCER

Surveillance
Intensive surveillance is meant to diagnose cancer at early stages, at which curative options exist. Surveillance for women at high risk of breast cancer consists of monthly self-breast examination, annual clinical breast examination, and mammography, ultrasound or MRI screening of the breasts. The reason for mammography annually instead of three years as in sporadic breast cancer, is that the growth rate of hereditary breast cancer in younger women is often faster [27, 28]. A problem with mammography is that the sensitivity in mutation carriers is significantly lower than in the general population due to the relatively dense breast parenchyma in younger women, and to the frequently benign appearance of BRCA-associated cancers on mammography [29, 30]. MRI has been shown to be superior to mammography in detecting breast tumors, although specificity is reduced and false-positive rates are increased [31]. In high-risk women, radiation from mammography may increase the risk of breast cancer later in life [32]. Ovarian cancer surveillance consists of transvaginal ovarian ultrasound and measurement of CA-125 levels but is controversial since the ability to find ovarian cancer at an early stage with these methods is small [33-35].

Bilateral prophylactic mastectomy
Bilateral prophylactic mastectomy (BPM) is the most effective method for reducing the risk of breast cancer and can reduce the risk by 95-100% in high-risk patients [36, 37]. Few cases are described in the literature of breast cancer after BPM [36, 38]. Using the reported number of risk reduction operations, Hamm et al. estimated that six patients would have to be treated with BPM to prevent a single breast cancer, and 25 patients would have to undergo BPM for every death prevented [39]. Besides reducing breast cancer risk, BPM has also been shown to significantly reduce patient anxiety about developing breast cancer [40-43]. BPM is an extensive surgical procedure, and aside from the risks of surgical complications, results in loss of an integral function of the female body, i.e. breast-feeding. However, although some women develop body image and sexuality problems after BPM [3, 41, 44-47], most women who undergo BPM are satisfied with their decision [45, 48].
Prophylactic salpingo-oophorectomy
Bilateral prophylactic salpingo-oophorectomy (BPSO) reduces the risk of breast cancer up to 50% by decreasing production of reproductive hormones [49]. However, even a 50% reduction constitutes a relatively high residual risk for BRCA1/2 mutation carriers. BPSO reduces ovarian cancer risk by more than 90% in BRCA1/2 mutation carriers [49], so these women may consider BPSO after completing childbearing. The immediate negative effects of BPSO are onset of menopausal symptoms such as hot flashes, sleep disturbances, anxiety, and depression, while long-term effects include decreased libido, vaginal dryness, and bone demineralization [50, 51]. Nearly all women experience some problems but the severity of these symptoms varies greatly.

Reduction mammaplasty
Women with a history of reduction mammaplasty have been shown to have up to a 30% reduced risk of breast cancer [52-54]. Reduction mammaplasty may be an option for women with large breasts and with only slightly increased risk of breast cancer, but it is not an option for known mutation carriers due to the limited reduction in risk.

Chemoprevention
The role of chemoprevention with selective estrogen receptor modulators (tamoxifen and raloxifene) in reducing the risk of breast cancer remains controversial. Existing data show that most BRCA1 and many BRCA2-associated breast cancers are estrogen-receptor-negative, meaning that estrogen receptor modulators are unlikely to reduce the risk [55]. Treatment with tamoxifen and raloxifene are also associated with increased risk of thrombotic vascular events (pulmonary embolism, stroke, deep venous thrombosis), cataracts and endometrial cancer (tamoxifen)[56].

Options at Karolinska University Hospital
Since the early 1990s, BPM and BPSO have been performed regularly at the Karolinska University Hospital which now handles about 50% of all BPM’s and IBR in Sweden. Patients with suspected inherited breast or ovarian cancer, or family members with a suspected increased risk of breast/ovarian cancer, are offered genetic counseling and if possible, mutation screening. High risk women (35-40% risk or higher) and mutation carriers are informed about the opportunities for inclusion in surveillance programs or for BPM and/or BPSO. Reduction mammaplasty may be offered to some women with large breasts and only a slight increased risk of breast
cancer. The women interested in prophylactic surgery are discussed by a multidisciplinary team consisting of a geneticist, oncologist, gynecologist, breast surgeon, plastic surgeon, psychologist and a contact nurse. All women who consider BPM are referred to a psychologist for at least one consultation during the decision-making process.

At Karolinska University Hospital, about more than half of the young women with BRCA1 or BRCA2 as well as some high-risk individuals with undetectable mutations choose to undergo bilateral prophylactic mastectomy at some point while almost all BRCA1- or BRCA2-mutation carriers choose to undergo BPSO after completing childbearing [57]. The proportion of high-risk women who undergo prophylactic procedures differs between countries and cultures. In a population in the Netherlands Meijers-Heiboer et al. reported that 51% of BRCA1/2 mutation carriers chose to undergo BPM, while 64% underwent BPSO, and parenthood was a predictor for choosing BPM, and higher age was associated with the decision to undergo BPSO. [58].
Bilateral prophylactic mastectomy

A BPM is almost always combined with an immediate breast reconstruction, and the two procedures are performed by a team consisting of a breast surgeon and a plastic surgeon. Many surgeons, plastic surgeons and oncologists involved in BPM advocate total mastectomy with resection of the nipple-areola complex (NAC) to guarantee removal of as much breast tissue as possible, in order to maximize risk reduction for the patient. However, in the last decade, the skin-sparing mastectomy has been widely accepted in breast cancer surgery and is today the recommended type of mastectomy for prophylaxis. Preserving the NAC in women undergoing prophylactic mastectomies and in selected patients with breast cancer has been widely debated. Patient satisfaction with preserved nipple-areola complexes in breast reconstruction after breast cancer surgery has been found to be very high [59-61], and Didier et al. have reported improved patient satisfaction with this procedure [62]. However, the removal of breast tissue is not as extensive as possible but several studies have confirmed the oncological safety of this procedure [59, 63-65]. It remains important to inform the patient preoperatively that sparing the NAC may lessen the risk reduction achieved with BPM. The goal of a prophylactic skin-sparing mastectomy is to remove as much breast tissue as possible without jeopardizing the blood-circulation of the skin. The dissection is performed just underneath Scarpa fascia, leaving skin-flaps of about 5-8 mm in thickness, extending cranially to just below the clavicle, laterally to the latissimus dorsi muscle border and extending inferiorly to the rectus abdominis muscle insertion on the ribs. Resection includes the axillary tail, and removed breast tissues, including a separate sample from the bases of the nipples, are sent for pathological examination.

All patients undergo pre-operative mammography and clinical breast examination before the BPM. Findings of invasive carcinoma in BPM specimen are rare. Premalignant and atypical findings are more common [66, 67] but routine use of sentinel node biopsy in patients undergoing BPM is not warranted [68, 69].

Different types of skin incisions can be used depending on the patient’s breast size and shape and on whether the NAC is to be spared or resected. In patients with small- to moderate-sized breasts, a periareolar skin incision that spares the NAC, or a horizontal...
skin excision including resection of the NAC, is often used. In patients with large or ptotic breasts where skin reduction is needed, a wise-pattern incision can be used including resection of the NAC. After NAC resection, the nipple tips may be regrafted at the end of surgery. They can later be removed if pathological examination of the nipple base shows malignancy or atypia. When NACs are resected, areolas are later tattooed to complete the reconstruction.

Skin-sparing mastectomy, horizontal skin incisions, resection of NACs, nipple tips are not regrafted.

Skin-sparing mastectomy, periareolar skin incisions with spared NACs.

Skin-sparing mastectomy, wise-pattern incisions with resection of NAC, nipples are regrafted at end of surgery
**Bilateral breast reconstruction**

Bilateral reconstruction can be performed with implants, autologous tissue or a combination of both. Due to the bilateral need, the autologous reconstruction is more challenging and hospital resource-intensive, which is why bilateral breast reconstruction is more often performed using implants alone [70-73].

**Implant-based reconstruction**

Bilateral implant-based reconstruction is a safe procedure with relatively short operating time (~3 hours), rapid recovery, no requirement for available tissue donor sites and no additional risk of complication or scarring at the donor sites. In an implant based reconstruction the implant is placed under complete or partial muscular cover. The reconstruction can be performed as a single-stage procedure, with immediate placement of expandable or permanent implants, or as a two-stage procedure with placement of an initial tissue expander followed by a secondary procedure for expander removal and placement of the permanent implant. Available implants are composed of a smooth or textured outer silicon shell, and filled with silicone gel, saline or a combination. If the implant is expandable a filling port is connected to the implant. Concerns about implant-based reconstruction include stability of the aesthetic result over time and the development of a fibrous capsular contracture around the implant.

**The shape of the implant**

Round shaped permanent expandable implants have been available for one-stage breast reconstruction after breast cancer surgery since the mid-1980s [74]. In the late 1980s, anatomically-shaped permanent expander implants were developed to further optimize the natural look of the reconstructed breast by a lower point of maximal projection, and therefore create a more prominent infra-mammary fold, less upper-pole fullness and a better match with the remaining contralateral breast in unilateral reconstructions [75-78]. Both anatomically-shaped and round implants have their surgical and aesthetic advantages and disadvantages, which may differ for a bilateral reconstruction vs. unilateral reconstruction in which symmetry with the remaining contralateral breast is one goal of the reconstruction. In the literature, there are a few studies evaluating anatomically-shaped versus round implants for bilateral breast augmentation [79, 80], but no randomized studies have evaluated implant shape in bilateral breast reconstructions.
Reconstruction with autologous tissue

In autologous breast reconstruction tissue is transferred from a donor site to the breast as a free flap using microsurgical technique, or as a pedicled flap. Autologous tissue gives a more natural consistency to the breast, as excised breast parenchyma is replaced with vascularized fat and/or muscle. The operating and recovery times are longer than after implant-based reconstruction, and severe complications, including pulmonary embolism, have been described, but are rare. Aesthetically, it is a long-lasting procedure and leaves no prosthetic material in the body.

The most commonly used flaps for autologous breast reconstruction are:

- The extended latissimus dorsi-flap (LD-flap), described by Marshall in 1984 [81]. The LD-flap is a pedicled flap commonly used for unilateral breast reconstruction of small to moderate-sized breast. A draw-back with the LD-flap is the necessity for intra-operative adjustments of the patient’s position as well as postoperative scarring on the back.

- Transverse rectus abdominis muscle flap (TRAM-flap), first described by Holmström in 1979 [82]. The TRAM-flap violates the rectus fascia and muscle, increasing the risk for donor site morbidity, such as abdominal wall weakness, bulging and hernia. The TRAM-flap can be either pedicled or free.

- The deep inferior epigastrica perforator flap (DIEP-flap), described by Koshima and Soeda in 1989 [83] is more difficult to harvest than the TRAM-flap since the rectus abdominal muscle is totally left in place. In Sweden, the DIEP-Flap is preferred since the risk of donor site morbidity is less than with the TRAM-flap. Prior abdominal surgery with midline, paramedian or subcostal scars restricts skin elasticity and may compromise donor site closure and vascularity in the donor sites for both TRAM- and DIEP-flaps.

- The transverse myocutaneous gracilis flap (TMG-flap) described by Wechselberger and Schoeller 2004. This flap is easy to harvest and leave discrete scars. [84, 85]. Another advantage with the TMG-flap is that the abdomen is left without scarring if the woman may want a future pregnancy.

- The superior gluteal artery perforator flap (SGAP-flap) described by Allen [86] is another option, but is more difficult to harvest, the pedicle is short and the fat is more dense and more difficult to shape. The SGAP-flap needs intra operative position change and leaves scarring and sometimes a visible volume defect on the bottom.
All autologous flaps can be combined with an implant to achieve additional breast volume. In bilateral autologous breast reconstruction at our department bilateral DIEP-flaps and bilateral TMG-flaps is preferred. There is no need for intra-operative position change, but the volume available may limit the ability to fully restore defects created by bilateral mastectomy, especially for large breasts.

**Implant-based vs. autologous breast reconstruction**

Implant-based breast reconstruction is the most commonly performed breast reconstruction procedure nationally and does not require a donor site. IBR with implants is perceived as less invasive compared to autologous flaps, requires a shorter convalescence, and does not use advanced microsurgical equipment. The risk of revision and implant exchange is, however, considerably high in the long-term [87-90]. The advantages of autologous reconstruction include absence of foreign material in the body and excellent long-term stability of the result after completion. Spear (2008) reported that patient satisfaction with implant reconstruction may be higher than breast reconstruction with autologous tissue despite higher reoperation rates and lower aesthetic scores [91].

Many women, especially younger patients who are more likely to be undergoing BPM, usually do not want lengthy autologous procedures with long hospital stay and convalescence. Autologous reconstruction after BPM might, however, be a better choice for a woman in whom implant-reconstructed breasts will not fit aesthetically with her body shape.

A higher prevalence of persistent pain in the breast after mastectomy followed by implant reconstruction (particularly sub-muscular placement) compared to autologous reconstruction or mastectomy without reconstruction has been reported by Wallace and Roth [92, 93]. On the other hand, autologous reconstructions risk the possibility of chronic pain at the donor site that is non-existent for implant-based reconstructions.
OUTCOMES AFTER BILATERAL PROPHYLACTIC MASTECTOMY AND IMMEDIATE BREAST RECONSTRUCTION WITH IMPLANTS

Sensitivity, pain and discomfort

Cutaneous breast sensitivity after mastectomy and reconstruction is probably an important component of patient satisfaction with the reconstruction, but has only been studied in breast cancer patients with quantitative methods [94, 95]. Several authors have confirmed that women ahead of prophylactic surgery need improved preoperative information about loss of sensitivity, feelings of discomfort and pain in the breasts and impact on daily life after BPM [1, 44, 96, 97].

Anatomical studies have shown that the dominant nerve supply to the breast and nipple-areola complex comes from the medial and lateral cutaneous branches of the third to fifth intercostal nerves [98, 99]. After a skin-sparing mastectomy and IBR the nerve supply is interrupted to the breast both subcutaneously and submuscularly. In cutaneous sensibility (the ability to feel touch, cold, warmth and painful cold and heat) three types of primary afferent fibers are activated by non-painful sensations and pain; large myelinated Aβ-(beta)-fibers (touch), small myelinated Aδ-(delta)-fibers (cold and pain) and small unmyelinated C-fibers (warmth and pain) [100]. Cutaneous sensibility, can be studied with Von Frey hairs [125] and quantitative sensory testing (QST). QST was developed to complement traditional neurological bedside examination, and its main advantage is greater precision in assessing functionality of somatosensory systems [101].

Chronic pain is a well-known side effect after different types of surgery [102, 103]. Bodily pain has also been reported as a common reason for sexual dysfunction in women [104, 105] The prevalence of chronic pain after breast cancer surgery has been reported to range from 20% to 68% [92, 106-109], and previous studies have suggested that young age, axillary surgery, damage to the intercostobrachial nerve, and radiation therapy are risk factors [108, 110-113].

Sexuality

The breasts are important sexual attributes and several studies in women undergoing prophylactic mastectomy have found that some experience a negative impact on sexuality and body image after surgery [3, 41, 44-47]; however, BPM is also reported to have a positive impact on body image and sexuality in some women [46, 96]. The negative impact on sexuality likely has several causes including sexual dysfunction due to hormonal deficits after prophylactic oophorectomy, unsatisfactory aesthetic outcome
from the breast reconstruction leading to poor body image and reduced self-confidence in sexual situations. Other possible causes to the negative impact on sexuality include loss of erogenous zones or pain and discomfort in the breasts.

**Quality of life**
The goal of breast reconstruction after BPM is primarily to improve the patient’s quality of life. The term “quality of life” refers to general wellbeing, and several definitions can be found in the literature. The term “health-related quality of life” refers specifically to aspects of life that are affected by health care interventions [114]. Health-related quality of life is often measured using questionnaires completed by patients themselves. A validated non-disease-specific questionnaire often used for medical interventions is the Short Form-36 (SF-36) [115], in which respondents are asked about their health over the past four weeks. The SF-36 has been adapted for a Swedish population (the Swedish Short Form-36), and Sullivan and Taft (2004) has shown that the Swedish version has good psychometric properties [116, 117]. Normative data for Swedish women are available [118]. In women undergoing BPM and IBR, Metcalfe et al., Geiger et al have reported that quality of life is not negatively affected but were than measured with other tools than SF-36 [119, 120]. Isern et al. have measured health-related quality of life and reported higher scores (=higher functioning) for women after BPM compared with a sample from the normal population [121]. Caffo et al. showed that pain after mastectomy due to breast cancer affected health-related quality of life negatively, measured by SF-36 [122].

**Feelings of regret**
Patients today are more involved in making their own health care decisions, and this is also true for women with high risk for breast cancer. In addition, the decision to undergo BPM is major and irreversible. Thus it is important that patients are well informed about the technical aspects, risks and benefits of alternative options so that feelings of regret can be avoided. It is important to understand the factors that contribute to regret after the decision to undergo BPM. A validated tool to measure regret after health care decisions is the Decision Regret Scale, which was developed by Brehaut et al. (2003) [123]. Mc Gauhey et al. and Van Oostrom et al. reported that most women who undergo BPM are satisfied with their decision [45, 48] but to our knowledge there are no existent data regarding feelings of regret in women after BPM without previous breast cancer diagnosis.
Aesthetic outcomes and patient satisfaction

The aesthetic outcome after the BPM and IBR is an important contributor to body image. Bresser and McGaughey have reported that dissatisfaction with the aesthetic outcome after BPM and IBR can negatively impact body image and have adverse effects on the woman’s sexual life [3, 45]. Satisfaction with the aesthetic result of BPM and IBR has been reported to range from 60-92% [3, 121, 124]. Further knowledge about patient satisfaction with aesthetic outcomes can be used to both improve the quality of preoperative information and suggest surgical refinements for future patients.
AIMS OF THE STUDIES

The main aim of this thesis was to investigate the outcomes after bilateral prophylactic mastectomy and immediate breast reconstruction with implants, in women with inherited risk of breast cancer development, and identify areas for improvement for future patients. The specific aims were:

- To evaluate somatosensory function in the reconstructed breasts and the patients’ subjective experience of breast sensitivity after BPM and IBR with implants, compared to a healthy, unoperated control group (I).

- To analyze the prevalence of persist pain and discomfort in the breasts and impact on sexuality, quality of life, and feelings of regret two years after BPM (II).

- To evaluate long-term aesthetic outcomes and patient satisfaction after BPM and IBR with implants (III).

- To compare BPM and IBR with expandable anatomically shaped implants vs. expandable round implants, with regards to implant-related complications, need for surgical correction, aesthetic outcome and patient satisfaction (IV).
PATIENTS AND METHODS

The four papers in this thesis include patients who underwent BPM and IBR with implants at the Karolinska University Hospital from 1993-2001 and 2004-2006. No patient developed breast cancer during the follow-up period.

PATIENTS

Paper I
Twenty-four patients who were treated from 1993-2001 and for whom at least two years had passed since their most recent surgery were included in this retrospective study evaluating breast sensitivity. The mean time since the BPM and IBR was five years (range 2-10). All women had undergone total mastectomy with NAC resection. Sixteen women who had no previous breast surgery comprised the control group.

Paper II
All (59) patients who underwent BPM and IBR between 2004-2006 were included in this retrospective questionnaire study. Time to follow-up was at least 2 years after BPM and IBR. All women had a skin-sparing mastectomy with either spared or resected NACs. The reference sample for quality of life measurements was comprised of 1725 women, aged 35-54 years, in the general Swedish population.

Paper III
Twenty-four patients who were consecutively operated on using a standardized procedure were included in this retrospective study, which evaluated aesthetic outcomes and patient satisfaction. All women had total bilateral mastectomy with resection of the NACs. Twenty-four healthy women without previous breast surgery, who were matched with respect to breast volume, served as the control subjects.

Paper IV
Thirty-six women operated on between 2004 and 2006 were included in this prospective, randomized study. All had undergone skin-sparing mastectomies with either spared or resected NACs. Outcomes of IBR with anatomically-shaped McGahn™ Style150 (Inamed/Allergan) or round shaped Siltex™ Becker25 (Mentor®) permanent expander implants were compared. Follow-up time was at least two years after BPM and at least one year after corrective procedure.
METHODS

SENSITIVITY, PAIN AND DISCOMFORT (I-II)
Based on the longstanding clinical observation that most somatosensory functions seem to recover in two years after nerve damage, time for evaluation of somatosensory function is preferred to include a minimum of two years after nerve damage or surgery.

Quantitative Somatosensory Testing (QST) (I)
The examinations were performed in a quiet room with the patient lying on a hospital bed. Two points on each breast were marked on the skin, 1 cm away from the border of the tattooed areola and at least 2 cm from any visible scar. Each point was examined for perception thresholds to touch, cold, warmth, and heat pain. A central point on the nipple was assessed only for sensitivity to touch.

Illustration of the patients included in study I, II, III and IV.

The position of measurement were located at the same positions in both patients and controls.
**Stimuli for touch**

Optihair von Frey Filaments (*MARSTOCK* nervtest, Marburg, Germany) [125] were used to assess the tactile perception threshold and function in low threshold A-beta afferents. The filaments (with nominal forces in (g) of 0.03-30 g) were applied to the skin, and prodded until they bent and were then withdrawn. The filaments were applied in a descending order of magnitude to assess the threshold at which sensation disappeared, and thereafter in ascending order to assess the threshold at which sensation reappeared. This procedure was repeated twice and the mean threshold value calculated. When none of the stimuli were detected, the sensitivity was recorded as the top (cut-off) value – that is, 30 g.

![Left: Von Frey filaments. Right: Apparature for MSA/Thermotest®.](image)

**Stimuli for cold, warmth and heat pain**

Quantitative testing of thermal sensitivity was performed by a unidirectional stimulation technique using a commercially available device with a Peltier element-based thermode of 18 x 18 mm, Modular Sensory Analyser, (MSA) Thermotest®[126]. All measurements started from skin temperature. First, the threshold for painless cold was assessed by delivering 5 cold stimuli at a rate of 1°C/second. The subject was instructed to press the button of a handheld switch to terminate the stimulus at the first sensation of cold. The mean of the assessments was calculated as the cold perception threshold. The cut-off level was 10°C, as the MSA Thermotest® is unable to keep a constant stimulus rate below this temperature. If the subject did not feel a cold stimulus at 10°C the recorded perception level was set equal to the cut-off value (10°C). The threshold for painless warmth was obtained in the same way by delivering 5 warm stimuli. If the subject did not experience warmth at 50°C the test was interrupted to avoid skin damage and the cut-off value of 50°C was recorded as the perception
threshold to warmth. After assessment of painless thermal perception, the heat pain level was assessed 3 times at a stimulus rate of 2°C/sec. The subject was asked to push the button and terminate the stimulus immediately when the heat sensation became painful. The maximum temperature was set at 50°C to avoid skin damage. The mean of the last two perception levels was calculated as the heat pain threshold.

**Patients’ subjective experiences (I-II)**

In paper I, a study specific questionnaire about subjective feelings in the reconstructed breasts, used in another study of somatosensory status after breast surgery [127] was answered by the patients and completed before the somatosensory examination. In paper II, the prevalence of pain and/or discomfort were assessed using study-specific questions regarding the presence of pain and discomfort in the breasts, trigger stimuli, pain quality, and impact on daily life or sleep. Patients who reported pain were asked to mark the affected areas on a drawing of the female upper body. The questionnaire was developed in collaboration with the Pain Center at the Department of Neurosurgery, Karolinska University Hospital and no formal validation or realiability testing has been performed.

**SEXUALITY (I-II)**

In the questionnaire regarding sensitivity used in paper I, one item was about the ability of sexual feelings in the reconstructed breasts and was answered by the patients. In paper II, sexuality was assessed with items concerning the breasts’ sexual importance for the patient before and after the BPM. These questions were followed by items concerning the ability to feel sexual sensations in the breast, changes in sexual attractiveness, sexual enjoyment, and sexual intercourse after the BPM. No formal validation or realiability testing has been performed on this questionnaire.

**HEALTH-RELATED QUALITY OF LIFE (II)**

Health-related quality of life was assessed using The Swedish Short Form-36 (SF-36), which consists of 36 items divided among eight domains: physical functioning, role limitations associated with physical problems, role limitations associated with emotional problems, bodily pain, general health, social functioning, vitality, and mental health. The mean scores for each of the domains were transformed to a 100-point scale, where high figures represent high functioning. The reference sample for quality of life measurements was comprised of 1725 women, aged 35 to 54 years, in the general
Swedish population also used in a previous study by Brandberg et al. assessing quality of life in women considering BPM and one year after BPM and IBR with implants [47, 128].

FEELINGS OF REGRET (II)
The Decision Regret Scale [123] was used to assess regret with respect to the decision to undergo BPM. The Decision Regret Scale has been shown to be a valid and reliable measure of satisfaction with health care decisions [123]. The Decision Regret Scale was translated into Swedish by one of the authors (J.G.) but no formal validation or reliability testing has been performed on the Swedish translation.

COMPLICATIONS AND CORRECTIONS (I-IV)
Information of surgical complications (i.e. skin-necrosis hematoma and implant loss due to infection) and corrective procedures were recorded from the journal files of the patients.

AESTHETIC OUTCOME AND PATIENT SATISFACTION (III-IV)
Zion et al. (2003) reported that among 593 women undergoing BPM and IBR, most corrective procedures after BPM took place within two years after the initial operation [89] and time to follow-up for the aesthetic evaluation was therefore in this thesis set to a 2-year minimum after the BPM. To ensure a stable aesthetic result, at least 12 months had to elapse after the latest corrective procedure.

Objective aesthetic evaluation
All patients and controls (III) participating in the objective aesthetic evaluations were examined at the out-patient clinic by the same examiner (J.G).

Breast volume
Preoperative breast volume and breast volume at follow-up was estimated using the thermoplastic cast technique ORFIT®, making a cast from the breast with the patient in an upright position for each breast. The impression in the cast from the breast was measured three times with water, and the mean volume was calculated. The thermoplastic cast system has been reported to be well tolerated by patients and have an acceptable error range in assessment of breast volume [129-131].
Breast symmetry
The symmetry according to breast volume and the breasts’ position on the thorax between the right and the left breast, was calculated by measuring the difference between the right and left breast. To determine symmetry regarding the breasts’ location on the thorax, the following distances were measured on both sides with the patient in an upright position: sternal notch to nipple, midline to nipple, sternal notch and infra-mammary fold. In study IV the distance nipple to infra-mammary fold was also measured.

Breast firmness (III)
Breast firmness was assessed with applanation tonometry [132-134], in which a Plexiglas disc was placed at the central part of the breast with the patient lying down. The contact area (A) between the disc and breast was calculated using the formula \( \pi ab/4 \), where (a) is the largest diameter and (b) the diameter perpendicular to (a) estimating the form of an ellipse. The weight of the Plexiglas disc is a known force (F), and the measured area (A) flattened by the force represents the intra-mammary pressure; this pressure can be estimated using the formula \( P=F/A \). Long-term development of breast consistency was calculated for patients in whom applanation tonometry had been performed at a one-year follow up examination after the initial surgery.
**Subjective aesthetic evaluation**

The aesthetic outcome was assessed by a blind expert panel that evaluated four standardized digital photograph views of each breast taken at follow-up. Two frontal views were shown, with the patients arms down in one and elevated to the horizontal plane in the other (to visualize the fourth “dimension” [135], and two oblique views with the projection of each breast.

In study III the expert panel consisted of two plastic surgeons. In study IV three plastic surgeons and a nurse specially educated in patients undergoing breast reconstruction were members in the expert panel. The plastic surgeons in the expert panels were not involved in the surgical procedures of the patients. The aesthetic assessment was made by showing the photographs on a computer screen. The assessed categories in study III were symmetry, volume, infra mammary fold, scarring and NAC. The final score for each aesthetic category was set by the calculated mean score from the expert panel. In study IV, each breast was first shown separately to avoid influence of the result of the contralateral reconstruction and for each separate breast the assessed categories were the appearance of shape, projection, upper-pole, infra-mammary fold, natural look and implant edges. Appearance of symmetry in shape, cleavage, scar tissue and overall aesthetic result were assessed with both the right and the left breast visible. In study IV, the expert panel was also asked to guess if the breasts were reconstructed with anatomically or round-shaped implants.
Examples of the photographic views used for assessment by the expert panel.

**Patient satisfaction**

In paper III, a study-specific questionnaire assessing satisfaction with the aesthetic outcome after breast reconstruction was sent to all patients by mail. This questionnaire had been used previously to study patients with breasts reconstructed with flaps [136], but had not been formally validated or tested for reliability. Patients completed the questionnaire before the examination, so as to prevent those results from influencing their responses to the questionnaire. The control group was not given the questionnaire. In paper IV, all patients received a study-specific questionnaire developed by the authors since to our knowledge no validated questionnaire existed that included all the aspects of aesthetic outcome we wanted to evaluate. The questionnaire has not been formally validated or reliability tested. In this questionnaire the patients assessed the shape of the right and left breast separately, while shape symmetry, scar tissue, overall aesthetic result, satisfaction with the overall aesthetic result and whether preoperative expectations were from outside to the bilateral aesthetic result. Lifestyle items regarding satisfaction with appearance in clothes, underwear, nudity and difficulty finding a well-fitting bra were also included in the questionnaire. Each question in the questionnaire was answered using a scale ranging from 1 (“Not at all”) through 7 (“Absolutely”), with a score of 4 considered “Acceptable.” This scale corresponded with the scale used in the expert panel’s assessment.

**ANATOMICAL VS. ROUND IMPLANT SHAPE (IV)**

The women were randomly assigned to reconstruction with anatomical or round implants and there were 18 women (36 breasts) in each group. We compared IBR with textured, short-height anatomically shaped, permanent expander implants McGahn™ Style150 developed by Inamed/Allergan and IBR with textured, round, permanent expander implants Siltex™ Becker25 developed by Mentor®.
All patients received implants of the same shape in the right and left breast. Aesthetic outcomes were evaluated objectively by symmetry measurements and subjectively by expert panel assessment and by patient self-report on a questionnaire. Both patients and the expert panel were blinded to which implants were used for reconstruction. To avoid denying future patients the most updated surgical procedures or technically refined implants, a maximum of three year was predetermined over which patients could be enrolled in the study. Information regarding surgical complications and corrective procedures were recorded from each patient’s medical file.

<table>
<thead>
<tr>
<th>Implant groups</th>
<th>Aesthetic evaluation</th>
<th>Anatomical (Style150) N=12</th>
<th>Round (Becker25) N=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (range)</td>
<td>38 (26-51)</td>
<td>39 (28-49)</td>
<td></td>
</tr>
<tr>
<td>Mean BMI (range)</td>
<td>22.2 (16.8-24.5)</td>
<td>23.8 (19.3-31.6)</td>
<td></td>
</tr>
<tr>
<td>Incision type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periareolar</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Horizontal/Oval</td>
<td>0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Wise-pattern</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

The representation of the different incision-types, BMI and age in the two implant groups.
STATISTICAL METHODS

Study I
Each value that corresponded to individual “yes” and “no” answers for the von Frey’s hairs was log transformed, because a non-linear relation exists between the von Frey hairs used. The arithmetic means were then anti-log transformed, creating a geometric mean, to visualize the results better in a graphic presentation. Wilcoxon signed ranks test was used to analyze touch thresholds comparing the four measure points and the heat pain levels within the groups. The Mann-Whitney test was used to analyze touch thresholds and heat pain levels. To analyse cold and warm thresholds within groups, a paired samples test was used. To analyze cold and warm thresholds between patients and controls, the independent samples test was used. To find out if there was any difference in the somatosensory function between the superior and inferior part of the reconstructed breast we used within-group analysis.

Study II
The statistical analyses performed aimed to evaluate outcomes of pain in the breasts, complications, changes in the breasts’ sexual importance, and sexual pleasure. Logistic regression, with a logit transformation of the outcome, was used to investigate the relationship between the outcomes and the independent variables (i.e., presence of pain, presence of discomfort, lost sexual sensitivity, sexual importance of the breasts before surgery, negative change in breast sexual importance, age, type of incision for mastectomy, complication and re-operation). A quadric term (e.g., age²) was added for each continuous predictor in the analyses to detect curve linear relationships. Due to the small sample size, a stepwise forward selection procedure was performed to decide which variables to include in the final model. An inclusion criterion of P < 0.05 was used. Variables of particular clinical importance were included regardless of their displayed P-values. A Student’s t-test was used to test for differences in health-related quality of life between the study sample and reference data.

Study III
Statistical analysis was performed using a paired samples test for analyzing the symmetry between the right and left breasts and an independent samples test for comparisons between the patient and control groups. In the breast measurements reflecting symmetry, the ratio between the right and left breast was calculated. The
ratios in the patient and control groups were then analyzed with an independent sample test. Significant differences were defined by p-values lower than 0.05.

Study IV

Statistical analysis was performed using a paired and unpaired t-test to compare the data between the two implant groups. Significant differences were defined by p-values lower than 0.05. The agreement between the members in the expert panel was measured with the weighted kappa measurement [137]. The kappa value and strength of agreement can be interpreted as follows: < 0.20 = poor, 0.21-0.40 = fair, 0.41-0.60 = moderate, 0.61-0.80 = good, 0.81-1.00 = very good.
SUMMARY OF RESULTS AND DISCUSSION

SENSITIVITY, PAIN AND DISCOMFORT (I-II)

In paper I, the outcome of von Frey hair testing showed reduced sensibility to touch in patients compared with controls (p<0.001) at all points of assessment and especially in the nipples. The ability to feel cold and warmth stimulus were also significantly reduced in patients compared with controls. The within-group analysis showed no systematic difference in the somatosensory function between the superior and inferior part of the reconstructed breast.

Results from paper I:
Significantly raised perception thresholds for touch, cold and warmth in patients (P) compared with controls (C) at measurement point 1(p1) and 2(p2) on the right (R) and left (L) breast. n= number of women in each group. (C) = degrees Celcius.

![Graphs showing touch thresholds to von Frey stimuli, perception thresholds to cold stimuli, and perception thresholds to warmth.](graphs.png)
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Mean follow-up years (range)</td>
<td>5.4 (2.4-10.2)</td>
<td>2.5 (2.0-4.1)</td>
</tr>
<tr>
<td>Mean age at BPM years (range)</td>
<td>42 (28-53)</td>
<td>40 (25-65)</td>
</tr>
<tr>
<td>Feelings of pain percentage of patients reporting</td>
<td>66%</td>
<td>69%</td>
</tr>
<tr>
<td>Feelings of discomfort percentage of patients reporting</td>
<td>66%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Comparison of results from the two study-specific questionnaires used in paper I and II. The questionnaire in paper II had a graded scale (1-7) in the answering alternatives and the questionnaire in paper I had yes/no as answering alternatives. (Appendix)

In paper II, the most frequent trigger stimuli were pressure and physical activity and the most common pain qualities were: aching, stinging, and cutting. The lateral part of the breast was the most commonly marked area of pain, and 36% of patients reported that pain affected their sleep, 22% their daily activities but only five patients reported occasional need for pain medication. The most frequent discomfort sensations were numbness, tingling, and squeezing triggered by touch, physical activity, or pressure.

Result from paper II: Illustration of the most frequently marked areas of feelings of pain. Darker color represents more frequently marked areas.
Cutaneous sensitivity after mastectomy and subsequent reconstruction with implants performed after breast cancer treatment has been studied previously by Benediktsson et al. and Lagergren et al. [94, 95]. There are also a few reports on the somatosensory status after breast reduction or reconstructive breast surgery with autologous tissue, and measured with different study methods [138-140]. The variability of study methods, and also different surgical methods, between prophylactic mastectomy and other types of breast surgery make it difficult to compare the results from paper I with previous reports of the somatosensory status.

The extensive nerve damage caused by a BPM is most likely responsible for the high prevalence of late post-operative pain and discomfort. A 60% prevalence of pain in the treated breast after unilateral mastectomy for breast cancer and with IBR using an expandable implant was previously reported previously by Gui et al. [76]. Our patients underwent a bilateral procedure, which might have been associated with an increased incidence of pain; it is positive to find that none of our patients reported severe pain.
SEXUALITY (I-II)
In paper I, 78% reported inability to feel sexual sensations in the reconstructed breasts. In paper II, the ability to feel sexual sensations in the breasts was reported to be completely lost in 45% of patients. This difference may exist because of the difference in the questionnaires answering alternatives (yes/no in paper I and graded 1-7 in paper II). In the graded scale in paper II, 40% of patients reported substantially impaired ability of sexual sensations and many of these might have answered “no” if the scale was not graded. The difference in the results from paper I and II may also be explained by that all patients in paper I underwent total mastectomy while in paper II all patients underwent skin-sparing mastectomy.
In paper II, the breasts were reported to be very important for sexuality before BPM for a majority of patients; after BPM, the sexual importance of the breasts changed in a negative way for 69%. The sexual enjoyment was reported to have changed in a negative way for 75% of the patients after the BPM. Patients reporting high sexual importance of the breasts before BPM, reported a negative impact on the breasts’ sexual importance after BPM (OR 5.71, \( P = 0.018 \)) and reduced enjoyment of sex (OR 6.14, \( P = 0.008 \)).
It might be of importance to discuss with the patient preoperatively the importance of the breast in her sexuality, since the risk of a negative impact on her sexual enjoyment is greater if the importance is high.
Surprisingly, there was no relationship between impaired or lost ability to feel sexual sensations in the breasts and reduced sexual enjoyment (OR 1.47, \( P = 0.671 \)). This finding indicates that sexual enjoyment after the BPM is focused on other erogenous zones on the body. The relationship between reduced sexual sensitivity and a negative change in the breasts’ sexual importance after BPM (OR 6.59, \( P = 0.064 \)) may confirm this theory. Although Paice and Ambler reported that pain is a common reason for sexual dysfunction in women [104, 105], no relationship between breast pain and a negative impact on sexual enjoyment was found in our study (OR 2.60, \( P = 0.514 \)).

BPSO surgery had at time of follow-up in study II been performed in 21 of 59 patients and had a relation with negative impact on sexuality (OR 4.88, \( P = 0.027 \)) but not with reduced sexual enjoyment (OR 1.81, \( P = 0.179 \)) when analyzed with age as a confounding factor for BPSO.
Results from questionnaire items regarding sexuality in paper II.

**HEALTH-RELATED QUALITY OF LIFE (II)**

Patients reported significantly higher mean scores in the bodily pain domain (i.e., less bodily pain) than did the control group ($P=0.002$), even though pain was frequently reported in the study-specific questionnaire. There were no statistically significant differences between patients and the reference sample in any of the other SF-36 variables. A possible explanation to the result in the domain bodily pain could be selection bias, in that women who seek out and undergo BPM are healthier than women in the general population.

The mean scores in the eight SF-36 subscales for the study and reference sample are presented on the next page. Comparable results regarding the health-related quality of life measured by the SF-36 after BPM have been presented previously [47, 121].
FEELINGS OF REGRET (II)

The results from the Decision Regret Scale showed very few feelings of regret, and no patient expressed agreement with the statement “I regret the decision I made”. Ten patients, however, expressed agreement or disagreement with the other statements. Of those ten patients, seven reported pain in the breasts, which is the same proportion as in the total sample. Complications requiring acute surgery due to hematoma or infection occurred in three patients, and six underwent bilateral implant exchange (a higher proportion than in the total sample). Stefanek et al. (1995) previously reported that experiencing a surgical complication was associated with dissatisfaction with the decision to undergo BPM [42].

Although BPM was associated with some negative effects, expression of regret was almost non-existent among our patients, which was consistent with reports from Bebbington-Hatcher et al. and Lloyd et al. [43, 96]. This finding indicates that for these women, relief at reducing the risk of breast cancer overrides the negative effects of BPM.
The results from the Decision Regret Scale. The percentage is shown inside the parenthesis.

### COMPLICATIONS AND CORRECTIONS (I-IV)

In patients operated on from 1993-2001 (I+ III), total mastectomies were performed (not skin-sparing), and no patient developed skin necrosis. In patients operated on from 2004-2006 (II and IV) all mastectomies were skin-sparing. The rate of skin-necrosis in these was 4% (two patients), which is consistent with rates in earlier studies on skin-sparing mastectomy and IBR with implants [69, 70, 90, 141, 142]. This illustrates the risk of skin-sparing mastectomy. The risk is probably elevated when the mastectomy is bilateral. The viability of skin flaps that cover fully inflated permanent implants is of concern and it has been described that placement of a partially deflated expander minimized the potential for exacerbating a compromised skin-flap [143]. Postoperative hematoma occurred in two patients operated on between 1993 and 2001 and in four patients operated on between 2004 and 2006. The rate of implant loss due to infection was 4% in both patient groups. Loss of an implant due to infection postponed reconstruction until a healing period of 4-6 months has passed.

To improve the final aesthetic result complementary corrective surgery was performed in 11/24 (46%) patients operated on between 1993 and 2001 and 35/59 (59%) of patients operated on between 2004 and 2006. These findings are consistent with Heemskerk-Gerritsen’s recently published report of long-term follow-up after BPM and IBR [69]. In patients operated on between 1993 and 2001, the most frequent complementary corrective surgery was correction of the NAC reconstruction. Even though NACs were spared in most patients operated on between 2004 and 2006, the incidence of corrective procedures was higher. This might be because women today
demand a better aesthetic result, or because plastic surgeons have raised the bar for an acceptable aesthetic outcome for a breast reconstruction. Therefore, patients should be informed preoperatively that an optimal cosmetic effect cannot be guaranteed after BPM and that corrective procedures are often needed to reach an acceptable aesthetic result.

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<tbody>
<tr>
<td><strong>Mean follow-up</strong></td>
<td></td>
<td></td>
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<tr>
<td>5.4 years (range 2.4-10.2)</td>
<td>Mean follow-up 2.5 years (range 2.0-4.1)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
<th>Total mastectomy (24)</th>
<th>Skin-sparing mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Hematoma</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Skin flap necrosis</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Corrective procedures</th>
<th>Periareolar incision (34)</th>
<th>Wise-pattern excision (20)</th>
<th>Horizontal excision (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsulotomy</td>
<td>3</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Implant exchange</td>
<td>2</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Scar correction</td>
<td>2</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Nipple–areola complex</td>
<td>6</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Liposuction</td>
<td>2</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Lipofilling</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Thoracodorsal flap</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal advancement</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of complications and types of corrective procedures in patients operated during 1993-2001 (total mastectomy) compared with patients operated during 2004-2006 (skin-sparing mastectomy).

In our department, placement of permanent expandable implants (a one-stage procedure) is preferred in bilateral breast reconstructions to spare the patient additional surgery to the implant pocket whenever possible. This is also preferable from the perspective of limited hospital resources. In one-stage procedures the plastic surgeon needs to be skilled as the goal is to avoid additional corrective procedures. One advantage of expandable implants is the ability to adjust the volume to meet patient’s desire and to correct volume asymmetry.

Complete muscular cover of the implant is attempted, as blood supplied by the covering muscle to the skin-flap together with the decreased internal compression from a partially-inflated expandable implant reduces the risk of partial or total flap necrosis [143-145]. Henriksen et al. showed that muscular coverage over the implant reduced the risk of severe capsular development [146]. Nevertheless, drawbacks still exists with this technique, including limited implant size and a greater difficulty to producing ptosis and a natural definition of the infra-mammary fold, even with the postoperative expansion process.
AESTHETIC OUTCOME AND PATIENT SATISFACTION (III-IV)

Objective aesthetic evaluation

In paper III, breast volumes did not differ between patients and controls with a matched breast volume. In paper IV, mean breast volumes were similar pre- and post-operatively but the range decreased. The mean breast volume increased with 35% in patients operated on between 2004 and 2006 (IV) compared with patients operated on between 1993 and 2001 (III). The larger breast volumes in the last series might come from that the mastectomies were skin-sparing or from that the patients’ personal wish was different. In paper IV, the range in breast volume decreased postoperatively and might be explained by that many women, especially those with a small preoperative breast size, desired to have a larger postoperative breast size after surgery and from the technical limitation in breast volume that can be achieved with implant based reconstruction. The degree of asymmetry between the right and left breast was small in patients operated on between 1993 and 2001 (III) and patients operated on between 2004 and 2006 (IV) with a mean positional asymmetry of less than 1 cm for 95% of patients. Asymmetry ratios calculated for the right and left breasts were equivalent to the non-operated controls in paper III and to patients’ preoperative measurements in paper IV. Despite the good symmetry the patients and expert panels in paper IV did not scored this parameter high, and it is possible that a slight breast asymmetry is more obvious in reconstructed breasts than in natural breasts.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean follow-up 5.4 years (range 2.4-10.2)</td>
<td>Mean follow-up 2.3 years (range 2.0-3.8)</td>
</tr>
<tr>
<td>Breast volume</td>
<td>Mean (range)</td>
<td>Mean difference right vs. left (range)</td>
</tr>
<tr>
<td></td>
<td>309 cc (124-712)</td>
<td>8 % (0-22)</td>
</tr>
<tr>
<td>Distance-measurements</td>
<td>(cm)</td>
<td>(cm)</td>
</tr>
<tr>
<td>Sternal notch - nipple</td>
<td>22.3 (20-29)</td>
<td>0.3 (0-1)</td>
</tr>
<tr>
<td>Sternal notch - infra mammary fold</td>
<td>28.6 (24-36)</td>
<td>0.5 (0-2)</td>
</tr>
<tr>
<td>Midline – nipple</td>
<td>11.1 (9-13)</td>
<td>0.5 (0-2)</td>
</tr>
</tbody>
</table>

Results from symmetry measurements in patients operated with 1993-2001 (total mastectomy) and patients operated 2004-2006 (skin-sparing mastectomy).
In paper III, breast firmness was evaluated in patients and compared with controls; patients had significantly smaller imprint areas in the applanation tonometry test showing that reconstructed breasts are much firmer than natural breasts. Long-term evaluation (mean 5.3 and range 2.1-8.4 years) of breast firmness could be performed in ten patients (20 breasts) and revealed that 19 out of the 20 breasts had become firmer compared with measurements obtained one year after BPM and IBR.

**Subjective aesthetic evaluation and patient satisfaction**

**Paper III**

In paper III, 83% (20/24) patients reported that the aesthetic result exceeded their expectations, and 92% (22/24) would recommend this type of breast reconstruction to another woman with hereditary risk of developing breast cancer. The results from assessments made by the expert panel and from the patient questionnaire were as follows:

<table>
<thead>
<tr>
<th>Patients’ opinion</th>
<th>Mean score</th>
<th>Plastic surgeons opinion</th>
<th>Mean score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of breast</td>
<td>3.9</td>
<td>Volume</td>
<td>4.7</td>
</tr>
<tr>
<td>Shape of breast</td>
<td>3.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Symmetry</td>
<td>4.0</td>
<td>Symmetry</td>
<td>4.7</td>
</tr>
<tr>
<td>Infra mammary fold</td>
<td>-</td>
<td>Infra mammary fold</td>
<td>4.8</td>
</tr>
<tr>
<td>Scars</td>
<td>4.4</td>
<td>Scars</td>
<td>4.7</td>
</tr>
<tr>
<td>Nipple - areola complex</td>
<td>3.6</td>
<td>Nipple-areola complex</td>
<td>4.9</td>
</tr>
<tr>
<td>Overall aesthetic result</td>
<td>5.0</td>
<td>Overall aesthetic result</td>
<td>4.7</td>
</tr>
</tbody>
</table>

*Scale 6 = excellent, 5 = good, 4 = acceptable, 3 = bad, 2 = very bad, (1 = not completed reconstruction)*

*Aesthetic outcome scores from the patients and the expert panel in paper III.*

The patients rated the aesthetic parameter “overall aesthetic result” highest. Plastic surgeons scored the aesthetic outcome of the nipple-areola complex most positively, but patient assessment of the outcome of this reconstruction was the most negative. This finding agrees with report from Jabor et al. [147] and indicates that patients and surgeons perceive the aesthetic result of the reconstructed NAC differently. Sparing the NAC in women undergoing bilateral prophylactic mastectomy is probably preferable despite the amount of breast tissue that will be left beneath it. It is, however important to emphasize to patients that a preserved NAC will most likely not maintain its
appearance and behavior in total as it usually become numb and loses the ability to respond to tactile stimuli due to transection of all sensory afferent fibers.

**Paper IV**

The category “shape-symmetry” had the highest mean score and “natural look” had the lowest in experts’ opinion. The strength of agreement between the assessments from members of the expert panel was moderate, with mean Kappa values between 0.36-0.57 indicating that professionals may have different opinions and preferences in aesthetic outcome after breast reconstruction.

All patients answered the questionnaire and the overall aesthetic result was assessed as good by the patients and as moderate by the expert panel. The patients were most satisfied with the appearance of the scars; this also received high mean scores from the expert panel. This is likely because mastectomies in the majority of patients in this paper were performed through peri-areolar incisions, which usually leave discrete scars.

<table>
<thead>
<tr>
<th>Appearance of:</th>
<th>Expert panel</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anatomical</td>
<td>Round</td>
</tr>
<tr>
<td></td>
<td>(Style150)</td>
<td>(Becker25)</td>
</tr>
<tr>
<td>Upper-pole</td>
<td>Mean score</td>
<td>Mean score</td>
</tr>
<tr>
<td>Projection</td>
<td>4.93</td>
<td>5.08</td>
</tr>
<tr>
<td>Infra-mammary fold</td>
<td>5.38</td>
<td>4.98</td>
</tr>
<tr>
<td>Natural look</td>
<td>4.42</td>
<td>4.04</td>
</tr>
<tr>
<td>Implant edges</td>
<td>4.44</td>
<td>4.61</td>
</tr>
<tr>
<td>Cleavage</td>
<td>4.92</td>
<td>5.07</td>
</tr>
<tr>
<td>Shape</td>
<td>4.58</td>
<td>4.42</td>
</tr>
<tr>
<td>Symmetry in shape</td>
<td>5.63</td>
<td>5.48</td>
</tr>
<tr>
<td>Scar tissue</td>
<td>5.46</td>
<td>5.34</td>
</tr>
<tr>
<td>Overall aesthetic result</td>
<td>4.71</td>
<td>4.27</td>
</tr>
</tbody>
</table>

Aesthetic outcome scores from the expert panel and comparison of the opinion of the aesthetic outcome scores between patients and the expert panel. Each parameter was assessed on a scale ranging from 1 through 7. Higher numbers represents better aesthetic result. (Appendix)

In the questionnaire 61%, (22/36) of patients reported that aesthetic result exceeded their expectations, and 47% (17/36) thought their reconstructed breasts were more beautiful than their former natural breasts. The mean scores for patients’ opinions about their breasts’ appearance in clothes or underwear were high (5.8 and 5.2 respectively) but appearance in nudity was scored much lower (mean = 3.9).
Left - before surgery. Right - after BPM through horizontal incisions and IBR with round implants. Nipples were regrafted and areolas tattooed.

Left - before surgery. Right - after BPM through periareolar incisions and IBR with anatomically shaped implants. NACs were spared.

Left - before surgery. Right - after BPM through Wise-pattern incisions and IBR with anatomically shaped implants. Nipples were regrafted and areolas tattooed.
ANATOMICAL VS. ROUND IMPLANT SHAPE (IV)

The average time to follow-up after BPM and IBR was 38 months (range 24-46). We found no statistical difference between the two implant groups in terms of complication rate, breast symmetry or outcome scores from the expert panel and patient assessments.

The risk of implant rotation is a known disadvantage with anatomically-shaped implants [148], and in the present study, 3/36 breasts (8%) had rotated.

In shape-related categories, the anatomically shaped implant received higher mean scores from the expert panel, while the round implants received higher mean scores from the patients. This suggests that patients and professionals have different preferences for optimal breast shape, which is consistent with Hsia’s findings in patients undergoing bilateral breast augmentation [149].

Illustration of outcome scores from patients vs. the expert panel in the shape-related categories and the overall aesthetic result.

In this study, there was only moderate agreement in the expert panel, indicating that even professionals have a different opinion when assessing aesthetic results. The absence of obvious differences in aesthetic outcome between anatomically-shaped and round implants for breast augmentations has been described by Friedman et al. [80] and is most likely explained by the impact from the overlying breast tissue covering the implant. In our material the breast tissue had been removed which shows that the shape of the breast is also affected from other factors as the degree of development of fibrous
capsule around the implant and pressure from overlying tissues, especially the muscles. An expandable implant is partially filled with saline and the shape might also be affected from gravity [79]. Rotation of an anatomically-shaped implant may also affect the shape of the reconstructed breast. In our study, the expert panel had difficulty recognizing implant shape used for the IBR. The rate of correct identification was 42% (range 17-50%) for anatomically-shaped and 66% (range 50-70%) for round-shaped implants, which was almost identical to rates described by Friedman et al. after bilateral breast augmentation [80]. The lack of any significant difference may depend on the relatively small sample; however, our results indicate no clear advantage or disadvantage with implants of either shape for a bilateral breast reconstruction.

Example of one patient where the expert panel guessed anatomically-shaped implants when the patient had round implants, indicating the difficulty in guessing the implant shape.

Example of one patient where the expert panel guessed round implants when the patient had anatomical shaped implants, indicating the difficulty in guessing the implant shape.
STUDY DESIGN CONSIDERATIONS

In paper I, results might have been limited by the small skin area investigated, but in the interest of time (i.e. ability for patients to concentrate ~2 hours), we restricted the number of measure points to six. In addition, sexual feelings were not assessed due to methodological problems.

The use of study-specific questionnaires that have not been formally tested for validity or reliability is a limitation for all four papers. At the time of these studies we knew of no formally validated questionnaires in the literature that covered the problems we were interested in. Response rates to our study-specific questionnaires were however very high, 88-100%.

The response rate on the SF-36 in study II was low, (64%) and thus at risk for selection bias. The women in paper II had been asked by mail to respond to the same questionnaire on three previous occasions (before BPM, and at six months and one year after BPM) during follow up for another study [47]. One reason for the lack of responses could be that these women were tired of being asked the same questions again such a long time after primary surgery. However, comparable results with higher response rate regarding the health-related quality of life measured by the SF-36 one year after BPM have been presented previously [47].

The study sample in paper I and III were small even though patients operated in a long time period was included. Because of the small number of women that undergo BPM annually, it is difficult to collect large materials and especially when a standardized surgical procedure is warranted in the study design.

In paper IV, the study sample was also small, which could explain why no significant difference was seen between the two implant shapes. Many women opting for BPM and IBR between 2004 and 2006 had a preconceived preference of “the best” implant shape and did not wanted to be included in a randomized study evaluating implant shape. In the aesthetic category “projection of the breast”, the p-value was 0.0742. When a post-hoc power analysis was run (nQuery Advisor, Statistical Solutions Ltd) using the estimates from the "projection" category, a two-sided hypothesis, risk level of 5% and power of 80%, 2 x 59 patients would have been needed to detect this difference.
CONCLUSIONS

Our results in this thesis on women undergoing bilateral prophylactic mastectomy and immediate reconstruction with implants showed that:

Cutaneous breast sensitivity is significantly impaired. Feelings of discomfort and/or slight pain are present in many women for a long time after surgery.

The ability for sexual sensations in the breast is often lost, and sexuality is negatively affected for a majority of women. If the breasts are considered very important in sexuality before BPM there is an increased risk of reduced enjoyment of sex after surgery.

Quality of life does not seem to be affected, and feelings of regret about the decision to undergo a bilateral prophylactic mastectomy are almost non-existent.

For 40% of the women BPM and IBR with expandable implants is a single stage-procedure. Corrective procedures are needed in 60% of patients to achieve satisfactory aesthetic results. No patient developed a severe surgical complication.

Results for breast symmetry after IBR with implants are equivalent to that of non-operated women. Patients are satisfied with the overall aesthetic result and reconstruction of the NAC seem to be an important area for surgical refinements in the future.

The patients and the plastic surgeon may have different preferences for breast shape. It is therefore important to determine patient preferences before surgery. Anatomically-shaped and round implants give comparable aesthetic results. The risk of implant rotation should be considered when anatomical implants are used.

In our opinion, these studies provide additional insights into the issues investigated here, as measured objectively and subjectively. This knowledge is important to address in consultations with women considering bilateral prophylactic mastectomy and IBR with implants and may help the women in their complex process of decision-making.
FUTURE PERSPECTIVES AND RESEARCH

Future progress in gene technology may possible change the management of women with inherited increased risk for breast cancer development.

BPM surgery is the most risk-reducing option available today, but in the future maybe more tailor-made surveillance or non-surgical treatments will be an option for high-risk patients.

The quality of the genetic counseling, psychological support before the decision to undergo BPM as well as the quality of BPM and effectiveness of tissue removal may probably vary. Most likely, the best counseling, psychological support, prophylaxis and outcomes will come from centers with large experience in taking care of these patients. Managing treatment in women with high estimated risk for breast cancer should probably be localized to a few specialized centers in countries with a small population as in Sweden’s.

Since there is still no consensus about preserving the NAC in this particular group of patients’ further studies that assess the oncological risk and whether preservation of the NAC increases patient satisfaction and reduces the negative effects on body image are needed. Multi-center studies are needed to reach a sufficient number of patients to get significant results.

Further improvements in breast implant technology may in the future result in more stable aesthetic result over time. In implant-based breast reconstruction, several techniques to better preserve the natural ptosis of the breast have been developed in recent years, such as creating a dual-plane pocket or complementing the muscular cover with a local dermal flap or with bioprosthetic dermal tissue [91, 150, 151]. Using these techniques may also be a good option in BPM patients, but are still not evaluated for this group of patients.

Bilateral autologous flaps may be performed more often in the future in these women as microsurgical techniques are becoming more standardized and safe.
Lipofilling to repair radiotherapy-induced tissue damage and to correct contour deformities after breast reconstruction with implants or autologous tissue is already established at many departments [152, 153], but the mechanisms and effects on the surrounding biologic milieu when this procedure is used in large populations are still not well known; thus further studies are needed before application of large volumes (i.e. filling whole breasts) can be recommended in women with high-risk for breast cancer.

Body image and sexuality after BPM may be influenced by the reaction of the patient’s partner. Further studies regarding the family’s and partner’s role are important to identify strategies for minimizing the risk of negative effects for the patients.
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REFERENCES


57. Wasteson-Arver, B., Department of oncology Karolinska University Hospital, Solna Sweden.


APPENDIX

Questions for the patients in paper I

Do you experience discomfort or pain in your reconstructed breasts without touching them? Yes No

Do you experience discomfort or pain in your reconstructed breasts when you or another person are touching them? Yes No

Can you feel touch? Right: Yes No
Left: Yes No

Can you feel temperature? (warmth, cold) Right: Yes No
Left: Yes No

Do the reconstructed breasts feel like breasts? Right: Yes No
Left: Yes No

Can you feel sexual sensations in your reconstructed breasts? Right: Yes No
Left: Yes No

Questions for the patients in paper IV

What do you think about the shape of your breasts?
Right: Very ugly 1 2 3 4 5 6 7 Very beautiful
Left: Very ugly 1 2 3 4 5 6 7 Very beautiful

What do you think about the symmetry in shape between your right and left breast?
Right: Very bad 1 2 3 4 5 6 7 Very good
Left: Very bad 1 2 3 4 5 6 7 Very good

What do you think about the appearance of your scars on your breasts?
Right: Very bad 1 2 3 4 5 6 7 Very good
Left: Very bad 1 2 3 4 5 6 7 Very good

What do you think about the overall aesthetic result of your reconstructed breasts?
Very bad 1 2 3 4 5 6 7 Very good

What do you think about the appearance of your breast in clothes?
Very bad 1 2 3 4 5 6 7 Very good

What do you think about the appearance of your breast in underwear/bikini?
Very bad 1 2 3 4 5 6 7 Very good

What do you think about the appearance of your breast when you are naked?
Very bad 1 2 3 4 5 6 7 Very good

What do you think about the appearance of your breast now compared with before the breast surgery? More ugly 1 2 3 4 5 6 7 More beautiful
Does the appearance of your breast reach the expectations you had before the surgery?
Not at all 1 2 3 4 5 6 7 Better than expected

Is it difficult to find a bra that fit your breasts?
Very difficult 1 2 3 4 5 6 7 Not at all

**Questions for the expert panel in paper IV**

What do you think about the appearance of the upper-pole of the reconstructed breast?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the projection of the reconstructed breasts?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the appearance of the infra-mammary fold of the reconstructed breast?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the natural look of the reconstructed breast?
Right: Very natural 1 2 3 acceptable 5 6 7 Very unnatural
Left: Very natural 1 2 3 acceptable 5 6 7 Very unnatural

What do you think about the visibility of the implant edges on the reconstructed breast?
Right: To visible 1 2 3 acceptable 5 6 7 Not visible
Left: To visible 1 2 3 acceptable 5 6 7 Not visible

What do you think about the appearance of the cleavage?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the shape of the reconstructed breast?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the symmetry in the shape of the reconstructed breasts?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the appearance of the scars on the reconstructed breast?
Right: Very bad 1 2 3 acceptable 5 6 7 Very good
Left: Very bad 1 2 3 acceptable 5 6 7 Very good

What do you think about the overall aesthetic result of the reconstructed breast?
Right: Very bad result 1 2 3 acceptable 5 6 7 Very good result
Left: Very bad result 1 2 3 acceptable 5 6 7 Very good result

What do you think about the shape of the implants do you think this patient have? Anatomically shaped implants
Round