



HAL
open science

Quality of life after immediate breast reconstruction and skin-sparing mastectomy - a comparison with patients undergoing breast conserving surgery

H.M. Heneghan, R.S. Prichard, R. Lyons, P.J. Regan, J.L. Kelly, C. Malone,
R. Mclaughlin, K.J. Sweeney, M.J. Kerin

► To cite this version:

H.M. Heneghan, R.S. Prichard, R. Lyons, P.J. Regan, J.L. Kelly, et al.. Quality of life after immediate breast reconstruction and skin-sparing mastectomy - a comparison with patients undergoing breast conserving surgery. *EJSO - European Journal of Surgical Oncology*, 2011, 37 (11), pp.937. 10.1016/j.ejso.2011.08.126 . hal-00738718

HAL Id: hal-00738718

<https://hal.science/hal-00738718v1>

Submitted on 5 Oct 2012

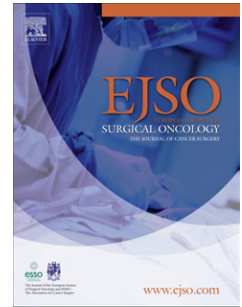
HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Accepted Manuscript

Title: Quality of life after immediate breast reconstruction and skin-sparing mastectomy – a comparison with patients undergoing breast conserving surgery

Authors: H.M. Heneghan, R.S. Prichard, R. Lyons, P.J. Regan, J.L. Kelly, C. Malone, R. McLaughlin, K.J. Sweeney, M.J. Kerin



PII: S0748-7983(11)00522-1

DOI: [10.1016/j.ejso.2011.08.126](https://doi.org/10.1016/j.ejso.2011.08.126)

Reference: YEJSO 3206

To appear in: *European Journal of Surgical Oncology*

Accepted Date: 22 August 2011

Please cite this article as: Heneghan HM, Prichard RS, Lyons R, Regan PJ, Kelly JL, Malone C, McLaughlin R, Sweeney KJ, Kerin MJ. Quality of life after immediate breast reconstruction and skin-sparing mastectomy – a comparison with patients undergoing breast conserving surgery, *European Journal of Surgical Oncology* (2011), doi: 10.1016/j.ejso.2011.08.126

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Title: Quality of life after immediate breast reconstruction and skin-sparing mastectomy – a comparison with patients undergoing breast conserving surgery

Short title: Quality of Life after Immediate Breast Reconstruction

Authors: HM Heneghan^{1§}, RS Prichard¹, R Lyons¹, PJ Regan², JL Kelly², C Malone¹, R McLaughlin¹, KJ Sweeney¹, MJ Kerin¹.

Affiliations: ¹ Department of Surgery, National University of Ireland, Galway, Ireland
² Department of Plastics & Reconstructive Surgery, Galway University Hospital, Galway, Ireland

[§]Corresponding Author: Dr Helen Heneghan

Address: Dept. of Surgery, National University of Ireland Galway.
Clinical Science Institute, Galway, Ireland

Email: helenheneghan@hotmail.com

Tel/Fax: +353 91 524390 / +353 91 494509

Abstract

Background: Historically breast cancer surgery was associated with significant psychosocial morbidity and suboptimal cosmetic outcome. Recent emphasis on women's quality of life following breast cancer treatment has drawn attention to the importance of aesthetic outcome and potential benefits of immediate breast reconstruction (IBR). Our primary aim was to assess patient's quality of life after IBR, compared to a matched group undergoing breast conservation. We also investigated the oncological safety and morbidity associated with immediate reconstruction.

Methods: A prospectively collected database of all breast cancer patients who underwent IBR at a tertiary referral breast unit was reviewed. Patients were reviewed clinically, and administered two validated quality of life questionnaires, at least one year after completing their treatment.

Results: 255 patients underwent IBR following mastectomy over a 55 month period. Reconstruction with ipsilateral latissimus dorsi flap was most commonly performed (88%). After mean follow-up of 36 months, IBR patients' quality of life was comparable to a group of age-matched women (n=160) who underwent breast conserving surgery (p=0.89). No patient experienced local recurrence (0%), distant metastases developed in 4.8% and disease related mortality was 2.2%. Post-operative morbidities included wound infection (11.8%), chronic pain (2.0%), capsular contracture (11%; 36% of whom had radiotherapy) and fat necrosis (14.1%). No patient experienced flap loss.

Conclusions: IBR is a highly acceptable form of treatment for women requiring mastectomy. With high rates of patient satisfaction, low associated morbidity, and proven oncological safety, it is an appropriate recommendation for all women requiring mastectomy.

Key words: immediate breast reconstruction; quality of life; skin-sparing mastectomy; breast conserving surgery; oncological outcome; breast cancer.

Note: This work was presented, in part, at the 2010 British Breast Cancer Research Conference, Nottingham, UK, 15-17th Sept 2010.

Introduction

The last decade has seen a paradigm shift in the management of breast cancer, toward less invasive diagnostic modalities and surgical approaches. This evolution occurred largely in response to an increased awareness of patients' psychosocial health and cosmesis following treatment for breast cancer. Breast conservation has now become the standard of care, where indicated [1]. However, up to one-third of breast cancer patients still require a mastectomy [2-3] and for these women, the practice of immediate breast reconstruction (IBR) may help to avoid the psychosocial morbidity and suboptimal cosmetic outcomes which were previously associated with mastectomy.

Since the first report of skin-sparing mastectomy and IBR in 1991[4], evidence has accumulated demonstrating its feasibility and acceptable outcomes. Its oncological safety has been well documented with several series reporting local recurrence (LR) rates in the range of 0-24% (Table 1). Benediktsson *et al* and Gerber *et al* have reported series with the longest follow-up to date; over 13 and 8 years respectively [5-6]. Therein, the respective authors document LR rates of 24% and 11%, which were comparable to LR rates in patients undergoing standard mastectomy without reconstruction. Further benefits of immediate reconstruction include superior aesthetic results, enhanced psychosocial outcome, and improved quality of life post treatment [7-12]. Despite these reported benefits, the delivery of IBR after mastectomy is still varied and influenced by surgeons' preferences rather than guided by available evidence [13-14].

NICE guidelines recently recommended that breast reconstruction be discussed with all women requiring mastectomy for early or locally advanced breast cancer [15]. However, these guidelines are presented with the caveat that for many outcomes, particularly psychosocial and patient-reported quality of life, the supporting evidence is relatively weak. Clearly, further data to support IBR is required. With regard to patient-reported outcomes (PRO), there has been little comparison between IBR and breast conserving surgery (BCS), which is considered the gold standard with regard to cosmetic outcome.

The primary aim of this study was to determine the quality of life of patients who underwent IBR following mastectomy at our tertiary referral breast cancer unit over a 5 year period, and compare with age and stage-matched patients who underwent BCS. We also wished to assess the oncological outcome and morbidity related to the reconstruction procedure.

ACCEPTED MANUSCRIPT

Patients and Methods

Patients

Ethical approval for this study was granted by the Galway University Hospitals' Regional Ethics Committee. All patients who underwent mastectomy followed by IBR at a tertiary referral breast cancer centre, between September 2004 and March 2009, were identified by searching a prospectively maintained breast cancer database. We also identified a similar sized cohort of age-matched breast cancer patients who underwent BCS in that same time period. This latter cohort represented an ideal comparative group for quality of life assessment following breast cancer treatment. A variety of demographic, clinical, and pathological data were obtained through review of the database, clinical and operative notes. All patients were treated according to local protocols and followed up weekly for the first 4-6 weeks or until seroma drainage was no longer necessary, then every 3 months for 1 year, 6 months for 2 years, and annually thereafter with clinical review and mammography.

Indications for mastectomy (with/without reconstruction) included tumor size >5cm, central sector tumor unsuitable for BCS, multiple tumor foci, relatively large tumor with respect to breast size, extensive high-grade in-situ carcinoma, inflammatory cancer, history of prior cancer in the breast, where radiotherapy is contraindicated, and patient preference. In the absence of all these factors, BCS followed by adjuvant radiotherapy was the treatment of choice. Patients with an indication for mastectomy were also offered IBR. All types of reconstruction, autologous and implant-based, were discussed with the patient. The informed patient's choice ultimately dictated the modality of reconstruction. In addition to being routinely administered after BCS, radiotherapy was also indicated in the following circumstances post-mastectomy and IBR [16]: microscopically involved margins in mastectomy specimen, ≥ 4 positive axillary lymph nodes, T3 tumors with positive axillary nodes, and operable stage III tumors. Occasionally, other tumor-related or patient-related factors suggestive of high risk for loco-regional recurrence or poor prognosis represented indications for post-mastectomy radiation. The decision to administer post-mastectomy radiation was made by a multi-disciplinary team, inclusive of breast surgeons and radiation oncologists. Ethical approval for this study was granted by the Galway University Hospitals Research Ethics Committee, and all patients consented to participate.

Surgical procedures:

Following skin-sparing mastectomy, reconstruction was routinely performed using pedicled autologous flaps, namely the latissimus dorsi flap (LD) with an underlying silicone prosthesis, extended LD flap without implant, or transverse rectus abdominis myocutaneous flap (TRAM). In a small number of cases, a prosthesis-only reconstruction was performed.

Outcomes assessed:

Primary endpoints were patient-reported quality of life and satisfaction with outcome after treatment. Secondary endpoints included LR rates and morbidity associated with IBR. Morbidities recorded included flap loss, bleeding complications, wound infection (breast and back wounds), clinically significant fat necrosis (defined as a persistent palpable abnormality on serial clinical examinations), capsular contracture, and chronic pain. Only modified Baker Class IV capsular contractures were recorded, as these were the only cases where aesthetic outcome was compromised to a degree where surgical intervention was indicated for revision [17].

Quality of life assessment

All IBR patients were contacted and asked to complete two validated self-administered, breast cancer-specific quality of life questionnaires; the EORTC-QLQ-B23 (coupled with the generic core EORTC-QLQ-C30, version 3.0) and FACT-B instruments. Questionnaires were returned by post. To increase the response rate patients were contacted by telephone as a reminder to complete and return questionnaires. The time-point for quality of life assessment was 12 months (± 3) following completion of adjuvant chemo-radiotherapy, or an equivalent time-point for patients who did not receive adjuvant therapy.

Statistical analysis

Data were analysed using questionnaire specific scoring systems, and SPSS software (PASW 18.0 for Windows). Both the number of observations and percentages are presented to describe categorical variables such as LR and morbidity rates. Differences in outcomes between IBR and BCS patients were calculated by means of

two-sample t-test for all two sample comparisons, and the chi square test for binomial comparisons. A p-value of <0.05 was assumed to represent statistical significance.

ACCEPTED MANUSCRIPT

Results:***Patient characteristics and treatment details***

Over a 55-month period between September 2004 and March 2009, 255 patients underwent IBR in Galway University Hospital, representing 69.5% of all women undergoing mastectomy in that period. In total 262 reconstructions were performed; 7 patients underwent bilateral mastectomy with IBR, 5 of whom were undergoing prophylactic procedures because of a genetic predisposition to breast cancer, and 2 women had bilateral breast tumors. Mean follow-up was 36 months (Range 12-70). Tumor characteristics and details of adjuvant therapy are demonstrated in Table 2. Among this cohort, 18% of breast cancer patients had pre-invasive disease (n=45), and the majority had early stage cancers (n=204, 82%). The types of reconstruction performed were LD flap (n=230, 88% including 17 extended LD flaps), TRAM flap (n=16, 6%), implant only (n=16, 3%), and other autologous tissue flaps such as local flap procedures (n=16, 3%). Nipple-sparing mastectomy was performed in 18% (n=46). Forty-six percent of IBR patients received adjuvant chemotherapy following reconstruction; administration of treatment was delayed in two cases because of wound infection requiring antibiotic treatment and dressings. Adjuvant radiotherapy was administered to 102 women (41%) following reconstruction.

Quality of life assessment

All IBR patients and 203 age- and stage-matched BCS patients were sent the EORTC-B23 and FACT-B questionnaires. Response rate was 74% (179 from IBR group and 160 of the BCS patients). The EORTC-B23 questionnaire results are reported in three components: functional outcome, symptoms, and global health score. There was no significant difference identified between IBR and BCS patients for any of these three outcomes (Table 4). The FACT-B tool yields an overall quality of life score, on a scale from 0-144. Both IBR and BCS patients reported similarly high mean quality of life scores using this instrument (112.7 ± 20.1 and 113.3 ± 19.4 respectively, $p=0.801$, Table 4).

Impact of radiotherapy after IBR on quality of life

Of the IBR patients who returned quality of life questionnaires (n=179), 75 had received adjuvant radiotherapy. Comparing quality of life scores of patients who had received radiation, with those who did not, demonstrated no significant difference

between these two groups for any component of the EORTC-B23 or FACT-B questionnaires (Table 5).

Impact of type of reconstruction on quality of life

Comparing patients with an extended LD flap reconstruction (no implant), to those with autologous flaps and underlying implants, revealed that the EORTC-B23 global health score was higher in the extended LD group, although the difference was not statistically significant (mean scores 89.5 ± 6.4 vs. 75.9 ± 18.6 , $p=0.148$).

Impact of disease stage on quality of life after IBR

We aimed to determine whether the TNM stage of breast cancer affected patient's quality of life after IBR.

There was no significant correlation between disease stage and quality of life scores:

- EORTC-B23 global health score vs. disease stage; Pearson's correlation coefficient -0.002 , $p=0.982$.
- FACT-B quality of life vs. disease stage; Pearson's correlation coefficient 0.012 , $p=0.911$.

IBR patients with advanced stages of disease (TNM stages 3 and 4), reported similar quality of life scores to patients with early stage disease (TNM stages 1 and 2), illustrating the psychosocial benefits of this procedure in patients with a poor prognosis.

Oncological outcome after mastectomy and IBR

At a mean follow-up of 36 months, there was no incidence of local or regional recurrence in any reconstructed breast. Distant disease progression occurred in 4.8% of women ($n=12$) and the mortality related to breast cancer was 2.4% ($n=6$). There were no peri-operative deaths in this series (within 30 days following IBR).

Morbidity associated with IBR

The overall reconstruction-related morbidity rate was 16.1% ($n=41$, Table 3). Thirty-one women experienced a single complication post-operatively whilst 10 patients had more than one adverse event. There was no case of partial or total flap loss in this series. Fat necrosis, wound infection, and capsular contracture were the commonest

IBR-related morbidities, occurring in 14.1% (n=36), 11.8% (n=30), and 11.0% (n=28) respectively. Of the 28 patients who developed a modified Baker Class IV capsular contracture, all had a prosthesis in-situ, and 10 (35.7%) of these patients had undergone radiotherapy following reconstruction. The rate of severe capsule formation among all patients who received radiotherapy was 9.8% (10 of 102 women), compared to 12.2% of patients who did not receive external beam radiotherapy (p=0.561). Of note, no patient with an extended LD flap developed significant capsule formation, despite the fact that 41% of this subgroup (7/17) received adjuvant radiotherapy.

Discussion

As breast cancer management evolved over the last decade, performing a radical mastectomy became less acceptable to patients and clinicians. The performance of BCS, as a safe oncological alternative to mastectomy, achieved excellent cosmetic results with associated improvements in patients' body image, well-being and quality of life [18]. The most significant corollary of a procedure as radical as a mastectomy is the suboptimal aesthetic result, which is known to have adverse psychosocial effects on breast cancer patients [2]. Evidence suggests that performing breast reconstruction for those women who require mastectomy can mitigate its negative consequences, and positively affect patients' quality of life [19-20]. Concerns that breast reconstruction may be associated with higher LR rates have also diminished in recent years, with the accumulation of evidence demonstrating its oncological safety.

There are several limitations with quality of life literature in this field to date, particularly the low level of evidence it provides due to individual studies small numbers and suboptimal design. Most authors have not consistently used validated or disease specific questionnaires in their assessments [21]. Mindful of this, we administered two validated disease-specific questionnaires to our IBR patients and to women in our unit who had the gold standard procedure for cosmesis, BCS. Our relatively large cohort of 255 IBR patients, 179 of whom completed quality of life assessment, allowed for subgroup analysis which yielded important information on the impact of radiotherapy, reconstruction type, and disease stage on quality of life. Although the duration of follow-up in our series is relatively short as yet, our results at this time support the oncological safety of IBR, with a 0% LR rate at mean follow-up of 36 months. We also demonstrate that IBR is associated with a low incidence of procedure-related morbidity.

Assessing patient reported outcomes (PRO), such as quality of life, in breast cancer patients is challenging. Many factors related to the diagnosis and treatment of breast cancer influence a woman's ability to cope with her disease, and impact on her well-being and psychosocial functioning. Using sensitive and disease-specific instruments to measure these outcomes is critical, but has not been widely practiced. The majority of quality of life studies in breast reconstruction patients have used generic questionnaires such as SF-36, linear visual analogue scales, or institution-derived

tools. In the absence of a suitable breast reconstruction specific instrument, we used a combination of breast-cancer specific questionnaires to improve the sensitivity and specificity of measuring quality of life in this unique population. The EORTC-B23 and FACT B instruments have both been validated, and have demonstrated reliability and clinical responsiveness [22-24]. Novel tools for measuring PROs in breast reconstruction patients are currently being developed, or going through validation processes. The BREAST-Q is one such questionnaire that measures satisfaction and surgery-related quality of life in patients undergoing mastectomy with and without reconstruction [25]. European collaborators are developing a breast reconstruction-specific PRO measure through the EORTC, and have completed the first two of four phases in the development of this 31-item module [26]. These advances will allow more accurate and sensitive measurements of breast reconstruction patients' psychosocial well-being in the near future.

Irradiating a reconstructed breast is one of the most contentious issues surrounding IBR and is often the primary reason oncoplastic breast surgeons delay reconstruction to a date when adjuvant therapy is complete. Radiation in this setting is known to impair wound healing, lead to fat necrosis, fibrotic changes, capsular contracture and suboptimal aesthetic outcome [27-28]. In this study, 41% of patients (n=102) who underwent IBR received adjuvant radiotherapy. This relatively high rate of postmastectomy radiation therapy reflects characteristics of our symptomatic patient population; 18% of our cohort had advanced stage 3 or 4 disease, the majority of patients were young (mean age 48.9 years) and 42% were node positive. Quality of life analysis demonstrated that patients who received radiation treatment after IBR had comparable scores to non-irradiated reconstruction patients. This suggests that from the patient's perspective, irradiating the reconstructed breast did not adversely affect their satisfaction with the procedure in a way that altered their quality of life. These findings are similar to those from the Michigan Breast Reconstruction Outcomes Study, in which general and aesthetic satisfaction was not significantly altered in reconstruction patients who received radiotherapy, irrespective of a higher complication rate in irradiated patients [29].

Significant capsule formation requiring capsulectomy and prosthesis replacement was observed in 9.8% of patients who received radiation post-reconstruction, compared to

12.2% of patients who did not receive external beam radiotherapy ($p=0.561$). Our rate of severe capsular contracture requiring intervention is less than that described by other groups, in both non-irradiated and irradiated patients. Reefy et al observed significant capsule formation in 85% of their irradiated reconstructions, compared to 13% of non-irradiated patients, at a mean follow-up time of 36 months [30]. Tran et al reported that 24% of 41 patients who underwent immediate TRAM flap reconstruction required an additional intervention to correct flap contracture after radiotherapy [31]. Factors that may have contributed to the low rate of capsule formation in our series, particularly among irradiated reconstruction patients, included minimizing the use of implants with autologous reconstruction [32]. Additionally, the radiation oncologists in our unit reduce the dose of radiation to 1.8 Gy per fraction in the presence of a reconstruction. A lower fraction, over longer duration, omitting boluses, and sparing the central part of the flap, are all modifications that may decrease injury to an autologous flap in a field requiring radiation treatment. Performing an extended LD flap in patients who require radiotherapy is an alternative means of decreasing the risk of capsular contracture. The extended LD flap provides sufficient volume to achieve an aesthetically pleasing reconstruction, whilst avoiding the need for an implant. In this series, 7 of 17 patients who underwent an extended LD reconstruction received adjuvant radiotherapy, and no morbidity was experienced in this subgroup. A further consideration is to employ an 'immediate-delayed' reconstruction technique for a woman who requires adjuvant radiotherapy. This involves placing a temporary sub-pectoral tissue expander at the time of mastectomy, and after radiotherapy is complete, performing a delayed reconstruction by replacing the expander with a myocutaneous flap and/or implant [30, 33].

Controversy surrounds the ideal timing of breast reconstruction. Historically, reconstructions were delayed to allow the patient adapt to and accept the deformity after mastectomy. It was thought she would then better appreciate the result of a reconstruction [2]. Delaying reconstruction until after adjuvant therapies were complete was also thought to be beneficial, particularly if patients required radiation treatment which was believed to compromise the viability of an autologous flap reconstruction. Postponing reconstruction was also thought to prevent any delays in the administration of adjuvant chemotherapy. However, immediate reconstruction has numerous potential advantages over the delayed approach. Among these are that it is

technically easier due to skin laxity and preservation of the infra-mammary fold, it obviates the need for a subsequent hospitalisation and anaesthetic, and is less costly [27].

In conclusion, the results presented here suggest that IBR is a highly acceptable form of treatment for women requiring mastectomy. It is associated with high quality of life, low procedure-related morbidity, and is oncologically safe. Hence, we believe immediate reconstruction is an appropriate recommendation for all women requiring mastectomy. Larger studies with longer follow-up are necessary to definitively demonstrate oncological safety and durability of patient satisfaction. As more specific quality of life instruments are developed, and well-designed multicentre trials evaluating PROs after IBR are completed, sufficient evidence will hopefully accrue to support IBR as the standard of care for patients requiring mastectomy.

Acknowledgements:

We gratefully acknowledge Ms. Catherine Curran for assistance with the collation of clinicopathological data. No financial support was obtained for this study.

Research funding

No funding was received for this study.

Conflicts of interest statement:

The authors have no commercial interests or financial ties to disclose and have no conflicts of interest related to this study.

References

- 1 Fitzal F, Gnant M. Breast conservation: evolution of surgical strategies. *Breast J* 2006;**12**:S165-73.
- 2 Cordeiro PG. Breast reconstruction after surgery for breast cancer. *N Engl J Med* 2008;**359**:1590-601.
- 3 Zork NM, Komenaka IK, Pennington RE, Jr., Bowling MW, Norton LE, Clare SE, et al. The effect of dedicated breast surgeons on the short-term outcomes in breast cancer. *Ann Surg* 2008;**248**:280-5.
- 4 Toth BA, Lappert P. Modified skin incisions for mastectomy: the need for plastic surgical input in preoperative planning. *Plast Reconstr Surg* 1991;**87**:1048-53.
- 5 Benediktsson KP, Perbeck L. Survival in breast cancer after nipple-sparing subcutaneous mastectomy and immediate reconstruction with implants: a prospective trial with 13 years median follow-up in 216 patients. *Eur J Surg Oncol* 2008;**34**:143-8.
- 6 Gerber B, Krause A, Dieterich M, Kundt G, Reimer T. The oncological safety of skin sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction: an extended follow-up study. *Ann Surg* 2009;**249**:461-8.
- 7 Anderson PR, Hanlon AL, Fowble BL, McNeeley SW, Freedman GM. Low complication rates are achievable after postmastectomy breast reconstruction and radiation therapy. *Int J Radiat Oncol Biol Phys* 2004;**59**:1080-7.
- 8 Cordeiro PG, Pusic AL, Disa JJ, McCormick B, VanZee K. Irradiation after immediate tissue expander/implant breast reconstruction: outcomes, complications, aesthetic results, and satisfaction among 156 patients. *Plast Reconstr Surg* 2004;**113**:877-81.
- 9 Drucker-Zertuche M, Robles-Vidal C. A 7 year experience with immediate breast reconstruction after skin sparing mastectomy for cancer. *Eur J Surg Oncol* 2007;**33**:140-6.
- 10 Gendy RK, Able JA, Rainsbury RM. Impact of skin-sparing mastectomy with immediate reconstruction and breast-sparing reconstruction with miniflaps on the outcomes of oncoplastic breast surgery. *Br J Surg* 2003;**90**:433-9.
- 11 Vandeweyer E. Peri-areolar skin-sparing mastectomy and immediate tram flap reconstruction. *Acta Chir Belg* 2003;**103**:219-24.
- 12 Vandeweyer E, Deraemaeker R, Nogaret JM, Hertens D. Immediate breast reconstruction with implants and adjuvant chemotherapy: a good option? *Acta Chir Belg* 2003;**103**:98-101.
- 13 Callaghan CJ, Couto E, Kerin MJ, Rainsbury RM, George WD, Purushotham AD. Breast reconstruction in the United Kingdom and Ireland. *Br J Surg* 2002;**89**:335-40.
- 14 Alderman AK, McMahon L, Jr., Wilkins EG. The national utilization of immediate and early delayed breast reconstruction and the effect of sociodemographic factors. *Plast Reconstr Surg* 2003;**111**:695-703; discussion 4-5.
- 15 Harnett A, Smallwood J, Titshall V, Champion A. Diagnosis and treatment of early breast cancer, including locally advanced disease--summary of NICE guidance. *BMJ* 2009;**338**:b438.
- 16 Recht A, Edge SB, Solin LJ, Robinson DS, Estabrook A, Fine RE, et al. Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2001;**19**:1539-69.

- 17 Spear SL, Baker JL, Jr. Classification of capsular contracture after prosthetic breast reconstruction. *Plast Reconstr Surg* 1995;**96**:1119-23; discussion 24.
- 18 Moyer A. Psychosocial outcomes of breast-conserving surgery versus mastectomy: a meta-analytic review. *Health Psychol* 1997;**16**:284-98.
- 19 Dean C, Chetty U, Forrest AP. Effects of immediate breast reconstruction on psychosocial morbidity after mastectomy. *Lancet* 1983;**1**:459-62.
- 20 Parker PA, Youssef A, Walker S, Basen-Engquist K, Cohen L, Gritz ER, et al. Short-term and long-term psychosocial adjustment and quality of life in women undergoing different surgical procedures for breast cancer. *Ann Surg Oncol* 2007;**14**:3078-89.
- 21 Winters ZE, Benson JR, Pusic AL. A Systematic Review of the Clinical Evidence to Guide Treatment Recommendations in Breast Reconstruction Based on Patient-Reported Outcome Measures and Health-Related Quality of Life. *Ann Surg* 2010.
- 22 Brady MJ, Cella DF, Mo F, Bonomi AE, Tulskey DS, Lloyd SR, et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. *J Clin Oncol* 1997;**15**:974-86.
- 23 Sprangers MA, Groenvold M, Arraras JI, Franklin J, te Velde A, Muller M, et al. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. *J Clin Oncol* 1996;**14**:2756-68.
- 24 Chen CM, Cano SJ, Klassen AF, King T, McCarthy C, Cordeiro PG, et al. Measuring quality of life in oncologic breast surgery: a systematic review of patient-reported outcome measures. *Breast J* 2010;**16**:587-97.
- 25 Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. *Plast Reconstr Surg* 2009;**124**:345-53.
- 26 Winters ZE, Thomson HJ. Assessing the clinical effectiveness of breast reconstruction through patient-reported outcome measures. *Br J Surg* 2011;**98**:323-5.
- 27 Chevray PM. Timing of breast reconstruction: immediate versus delayed. *Cancer J* 2008;**14**:223-9.
- 28 Mehta VK, Goffinet D. Postmastectomy radiation therapy after TRAM flap breast reconstruction. *Breast J* 2004;**10**:118-22.
- 29 Krueger EA, Wilkins EG, Strawderman M, Cederna P, Goldfarb S, Vicini FA, et al. Complications and patient satisfaction following expander/implant breast reconstruction with and without radiotherapy. *Int J Radiat Oncol Biol Phys* 2001;**49**:713-21.
- 30 Reefy S, Patani N, Anderson A, Burgoyne G, Osman H, Mokbel K. Oncological outcome and patient satisfaction with skin-sparing mastectomy and immediate breast reconstruction: a prospective observational study. *BMC Cancer* 2010;**10**:171.
- 31 Tran NV, Evans GR, Kroll SS, Baldwin BJ, Miller MJ, Reece GP, et al. Postoperative adjuvant irradiation: effects on tranverse rectus abdominis muscle flap breast reconstruction. *Plast Reconstr Surg* 2000;**106**:313-7; discussion 8-20.
- 32 Barry M, Kell MR. Radiotherapy and breast reconstruction: a meta-analysis. *Breast Cancer Res Treat* 2011.
- 33 Kronowitz SJ, Hunt KK, Kuerer HM, Babiera G, McNeese MD, Buchholz TA, et al. Delayed-immediate breast reconstruction. *Plast Reconstr Surg* 2004;**113**:1617-28.

- 34 Slavin SA, Love SM, Goldwyn RM. Recurrent breast cancer following immediate reconstruction with myocutaneous flaps. *Plast Reconstr Surg* 1994;**93**:1191-204; discussion 205-7.
- 35 Newman LA, Kuerer HM, Hunt KK, Kroll SS, Ames FC, Ross MI, et al. Presentation, treatment, and outcome of local recurrence after skin-sparing mastectomy and immediate breast reconstruction. *Ann Surg Oncol* 1998;**5**:620-6.
- 36 Rivadeneira DE, Simmons RM, Fish SK, Gayle L, La Trenta GS, Swistel A, et al. Skin-sparing mastectomy with immediate breast reconstruction: a critical analysis of local recurrence. *Cancer J* 2000;**6**:331-5.
- 37 Medina-Franco H, Vasconez LO, Fix RJ, Heslin MJ, Beenken SW, Bland KI, et al. Factors associated with local recurrence after skin-sparing mastectomy and immediate breast reconstruction for invasive breast cancer. *Ann Surg* 2002;**235**:814-9.
- 38 Carlson GW, Styblo TM, Lyles RH, Bostwick J, Murray DR, Staley CA, et al. Local recurrence after skin-sparing mastectomy: tumor biology or surgical conservatism? *Ann Surg Oncol* 2003;**10**:108-12.
- 39 Langstein HN, Cheng MH, Singletary SE, Robb GL, Hoy E, Smith TL, et al. Breast cancer recurrence after immediate reconstruction: patterns and significance. *Plast Reconstr Surg* 2003;**111**:712-20; discussion 21-2.
- 40 Spiegel AJ, Butler CE. Recurrence following treatment of ductal carcinoma in situ with skin-sparing mastectomy and immediate breast reconstruction. *Plast Reconstr Surg* 2003;**111**:706-11.
- 41 Foster RD, Hansen SL, Esserman LJ, Hwang ES, Ewing C, Lane K, et al. Safety of immediate transverse rectus abdominis myocutaneous breast reconstruction for patients with locally advanced disease. *Arch Surg* 2005;**140**:196-8; discussion 9-200.
- 42 Howard MA, Polo K, Pusic AL, Cordeiro PG, Hidalgo DA, Mehrara B, et al. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. *Plast Reconstr Surg* 2006;**117**:1381-6.
- 43 Meretoja TJ, Rasia S, Von Smotten KAJ, Asko-Seljavaara SL, Kuokkanen HOM, Jahkola TA. Late results of skin-sparing mastectomy followed by immediate breast reconstruction. *British Journal of Surgery* 2007;**94**:1220-5.
- 44 Omranipour R, Bobin JY, Esouyeh M. Skin Sparing Mastectomy and Immediate Breast Reconstruction (SSMIR) for early breast cancer: eight years single institution experience. *World J Surg Oncol* 2008;**6**:43.
- 45 Ueda S, Tamaki Y, Yano K, Okishiro N, Yanagisawa T, Imasato M, et al. Cosmetic outcome and patient satisfaction after skin-sparing mastectomy for breast cancer with immediate reconstruction of the breast. *Surgery* 2008;**143**:414-25.
- 46 Petit JY, Gentilini O, Rotmensch N, Rey P, Rietjens M, Garusi C, et al. Oncological results of immediate breast reconstruction: long term follow-up of a large series at a single institution. *Breast Cancer Res Treat* 2008;**112**:545-9.
- 47 Wirth R, Banic A, Erni D. Aesthetic outcome and oncological safety of nipple-areola complex replantation after mastectomy and immediate breast reconstruction. *J Plast Reconstr Aesthet Surg* 2010;**63**:1490-4.
- 48 Min SY, Kim HY, Jung SY, Kwon Y, Shin KH, Lee S, et al. Oncological safety and quality of life associated with mastectomy and immediate breast reconstruction with a latissimus dorsi myocutaneous flap. *Breast J* 2010;**16**:356-61.

49 *Lim W, Ko BS, Kim HJ, Lee JW, Eom JS, Son BH, et al. Oncological safety of skin sparing mastectomy followed by immediate reconstruction for locally advanced breast cancer. J Surg Oncol 2010;102:39-42.*

ACCEPTED MANUSCRIPT

Tables:

Table 1. Oncological safety of IBR for breast cancer: summary of existing reports ^a						
1 st Author	Year	N	Type of Reconstruction	Local recurrence (%)	Follow-up ^b (months)	TNM Stage
Slavin [34]	1998	51	LD	10.00%	45	Stage 0-2
Newman [35]	1998	372	TRAM, LD	6.20%	50	Stage 1-2
Toth [4]	1999	50	TRAM (58%), implant (42%)	0.00%	57	Stage 0-3
Rivadeneira [36]	2000	71	TRAM (48%), expander (52%)	5.60%	49	Stage 0-3
Medina-Franco [37]	2002	176	TRAM (92%), LD (2%), implant (6%)	4.50%	73	Stage 1-3
Carlson [38]	2003	539	Not stated	5.50%	65	Stage 0-4
Langstein [39]	2003	1694	TRAM (70%), LD (9%), implant (21%)	2.30%	80.8	Stage 1-2
Spiegel and Butler [40]	2003	221	TRAM (62%), LD (4%), implant (34%)	4.50%	118	Stage 0-2
Foster [41]	2005	252	TRAM	0.30%	48	Stage 1-4
Howard [42]	2006	419	TRAM	3.80%	59	Stage 0-3
Meretoja [43]	2007	207	TRAM (73%), LD (24%), implant (3%)	5.1%	70	Stage 0-3
Omranipour [44]	2008	95	TRAM (4.2%), LD (66.3%), implant (29.4%)	1.10%	69	Stage 0-2
Ueda [45]	2008	74	TRAM (7%), LD (59%), DIEP (32%) implant (2%)	5.00%	50	Stage 0-3
Benediktsson [5]	2008	216	Implant	24.10%	156	Stage 0-3
Petit [46]	2008	518	TRAM (5%), LD (1%), implant/expander (94%)	5.00%	70	Stage 1-3
Gerber [6]	2009	108	TRAM (37%), LD (63%)	11.10%	101	Stage 0-3
Wirth [47]	2009	52	TRAM/DIEP (44%) LD (54%) implant (2%)	1.10%	49	Stage 0-3
Min [48]	2010	120	LD	3.30%	39	Stage 0-3
Reefy [30]	2010	137	LD (63%) implant (37%)	0%	36	Stage 0-3
Lim [49]	2010	87	TRAM (85%) LD (2%) implant (13%)	4.60%	63	Stage 2-3

^a Excluding case reports and case series of <10 patients. Also excludes prior publications from a group of authors on the same patient population

^b Mean or median.

IBR: immediate breast reconstruction. DCIS: ductal carcinoma in-situ

Table 2. Characteristics of patients undergoing mastectomy and IBR (N=255)

		n (%)
Mean age (Range)	48.9 years (29 -75)	
Disease type	Invasive	205 (80)
	Non invasive	45 (18)
	None (prophylactic procedure)	5 (2)
Nodal Status ^c	Positive	105 (42)
	Negative	145 (58)
Hormone receptor status ^c	ER/PR positive	201 (80)
	Her2/ <i>neu</i> positive	53 (21)
Stage ^c	<i>in situ</i>	45 (18)
	I	76 (31)
	II	83 (33)
	III	43 (17)
	IV	3 (1)
Chemotherapy ^c	Neoadjuvant	35 (14)
	Adjuvant	114 (46)
	None	101 (40)
Adjuvant radiotherapy ^c	Yes	102 (41)
	No	148 (59)

^c Of 250 patients with histologically confirmed breast cancer

Table 3. Post-operative morbidity related to reconstruction (N=255)	
	n (%)
Flap loss	0 (0)
Infection	
Breast wound	28 (11.0)
Back wound	2 (0.8)
Capsule formation requiring capsulectomy and prosthesis replacement	28 (11.0)
<i>10 of these patients had radiotherapy after reconstruction</i>	
Fat necrosis	36 (14.1)
Chronic pain	5 (2.0)
Haematoma evacuation at LD flap harvest site	2 (0.8)

Table 4. Quality of life assessment: Comparison between IBR and BCS patients			
	IBR group	BCS group	<i>p value</i>
N	179	160	
Mean age (Range)	49 years (27-74)	50 years (30-74)	<i>0.379</i>
Mean Follow-up	36 months	35 months	<i>0.733</i>
Stage of disease, n (%)			
In-situ	30 (17%)	24 (15%)	
Stage I	43 (24%)	45 (28%)	<i>0.341</i>
Stage II	65 (36%)	72 (45%)	
Stage III	39 (22%)	18 (11%)	
Stage IV	2 (1%)	1 (1%)	
Adjuvant chemotherapy, n (%)	86 (48%)	85 (53%)	<i>0.350</i>
EORTC-B23, mean ± SD			
Functional score	78.1±13.4	81.2±12.6	<i>0.083</i>
Symptom score	13.8±12.0	14.1±11.4	<i>0.852</i>
Global health score	76.3±18.5	77.1±19.9	<i>0.797</i>
FACT-B, mean ± SD			
Overall FACT-B score ^d	112.7±20.1	113.3±19.4	<i>0.801</i>
General health (FACT-G score)	87.6±15.3	97.8±99.2	<i>0.346</i>
Breast specific score (TOI score ^e)	71.2±13.2	70.8±13.5	<i>0.814</i>

^d Breast cancer specific measurement

^e TOI: Trial outcome index is the sum of the scores from the 23 items in the FACT B questionnaire that make up the physical and functional well-being and the breast cancer specific subscales.

Table 5. Quality of life outcomes^f of IBR patients who had radiotherapy after reconstruction, compared to those who did not receive radiotherapy

	Radiotherapy	No radiotherapy	p-value
N	75	104	
EORTC-B23 (0-100)			
Functional score (0-100)	77.4 ± 13.0	78.6 ± 13.8	0.635
Symptom score (0-100)	14.9 ± 13.0	13.0 ± 11.2	0.419
Global health score (0-100)	72.7 ± 20.1	78.3 ± 17.1	0.112
FACT-B (0-144)			
Overall quality of life	111.0 ± 19.5	115.1 ± 19.3	0.258

^f mean scores ± SD