Jesensko strokovno srečanje Združenja za senologijo 2015

19.11. 2015

Hotel Plaza Ljubljana

Predavatelji:
Prof. dr. Janez Žgajnar, dr. med., Oddelek za onkološko kirurgijo, Onkološki inštitut Ljubljana
Prof. dr. Uroš Ahčan, dr.med., Klinični oddelek za plastično kirurgijo in opekline, UKC Ljubljana
Dr. Tanja Marinko, dr.med., Oddelek za radioterapijo, Onkološki inštitut Ljubljana
Dr. Simona Borštnar, dr. med., Oddelek za internistično onkologijo, Onkološki inštitut Ljubljana

Urednica zbornika:
Simona Borštnar

Organizator in izdrajatelj:
Združenje za senologijo pri SZD

Strokovno srečanje sta finančno omogočili podjetji AstraZeneca in Roche

Ljubljana, november 2015

PROGRAM STROKOVNEGA SREČANJA:

16.00-16.30	*Prihod udeležencev*
16.30-16.50	*Kdaj ohranitvena operacija raka dojk ni možna?* **Janez Žgajnar,** Oddelek za onkološko kirurgijo, Onkološki inštitut Ljubljana
16.50-17.10	*Kako danes rekonstruiramo dojko?* **Uroš Ahčan,** Klinični oddelek za plastično kirurgijo in opekline, UKC Ljubljana
17.10-17.30	*Rekonstrukcija dojke in obsevanje* **Tanja Marinko,** Oddelek za radioterapijo, Onkološki inštitut Ljubljana
17.30-17.50	*Novosti v predoperativnem zdravljenju raka dojk* **Simona Borštnar,** Oddelek za internistično onkologijo, Onkološki inštitut Ljubljana
17.50-18.15	Razprava
18.15	Večerja

Kdaj ohranitev dojke ni mogoča?

Janez Žgajnar
OI

Kaj so razlogi za tak naslov?

- Delež mastektomij še vedno visok
- Delež mastektomij celo raste
  - Uporaba MRI
  - Boljše tehnike in dostopnost rekonstrukcij dojk
  - Porast kontralateralnih profilaktičnih mastektomij

Review Article

Magnetic Resonance Imaging in Patients With Newly Diagnosed Breast Cancer

A Review of the Literature

Melissa Pilewskie, MD; and Tari A. King, MD

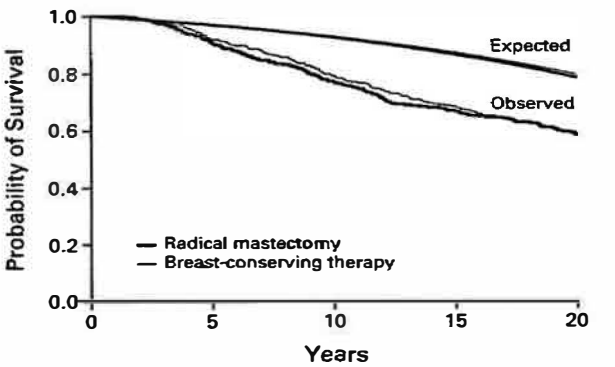
The use of magnetic resonance imaging (MRI) in patients with newly diagnosed breast cancer remains controversial. Here we review the current use of breast MRI and the impact of MRI on short-term surgical outcomes and rates of local recurrence. In addition, we address the use of MRI in specific patient populations, such as those with ductal carcinoma in situ, invasive lobular carcinoma, and occult primary breast cancer, and discuss the potential role of MRI for assessing response to neoadjuvant chemotherapy. Although MRI has improved sensitivity compared with conventional imaging, this has not translated into improved short-term surgical outcomes or long-term patient benefit, such as improved local control or survival, in any patient population. MRI is an important diagnostic tool in the evaluation of patients presenting with occult primary breast cancer and has shown promise in monitoring response to neoadjuvant chemotherapy; however, the data do not support the routine use of perioperative MRI in patients with newly diagnosed breast cancer. Cancer 2014;120:2655–64. © 2014 American Cancer Society.

KEYWORDS: magnetic resonance imaging (MRI), breast cancer, breast-conserving surgery, local recurrence

BCT je varna

Milan I trial

Veronesi, NEJM, 2002



Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*

Lancet 2011; 378: 1707–16

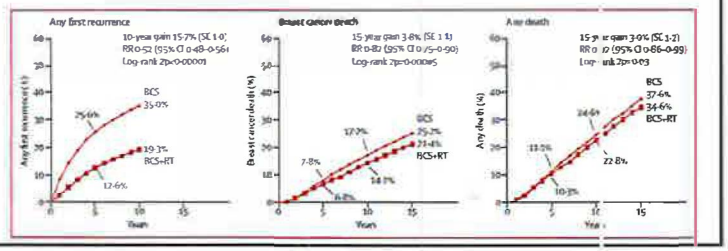


Figure 1 Timeline of landmark developments in breast cancer surgery

Wyld, L. *et al.* (2014) The evolution of cancer surgery and future perspectives
Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2014.191

nature REVIEWS CLINICAL ONCOLOGY

SMERNICE DIAGNOSTIKE IN ZDRAVLJENJA RAKA DOJK

LJUBLJANA 2014

OHRANITVENA OPERACIJA DOJKE

- **Indikacije**
  - ugodno razmerje med velikostjo tumorja in velikostjo dojke za zadovoljiv videz po operaciji
  - unicentričnost (lahko multifokalnost) bolezni
  - ni kontraindikacij za pooperativno obsevanje
- **Tehnika**
  - rez nad tipnim tumorjem, izrez tumorja z ustreznim varnostnim plaščem zdravega tkiva

ENOSTAVNA MASTEKTOMIJA[1]

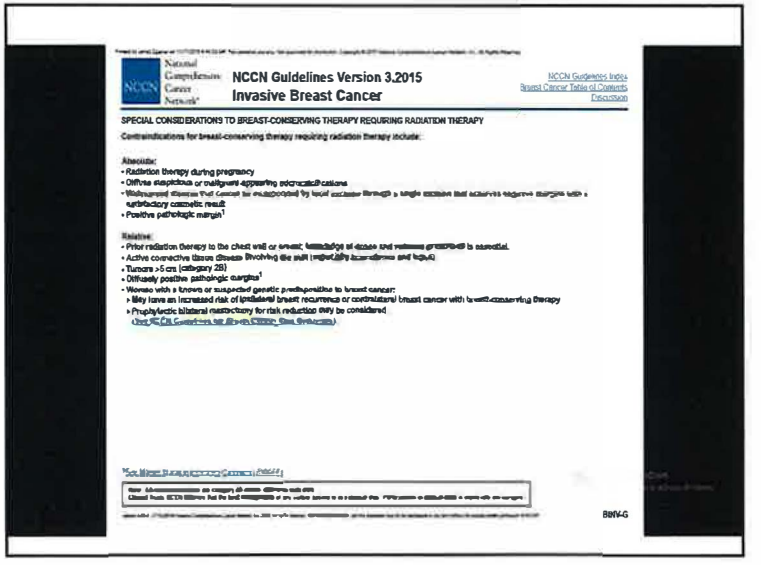
- **Indikacije**
  - neugodno razmerje med velikostjo tumorja in velikostjo dojke
  - multicentričnost (ne multifokalnost) bolezni
  - vnetni rak dojk po predoperativnem sistemskem zdravljenju
  - nosečnost v prvem trimesečju
  - kontraindikacije za pooperativno obsevanje
  - metastatski rak dojke (po sklepu multidisciplinarnega konzilija)

MASTEKTOMIJA Z OHRANITVIJO KOŽE

- **Indikacije**
  - za mastektomijo z ohranitvijo kože se odločimo, če opravimo istočasno še rekonstrukcijo dojke, sicer so indikacije enake kot za enostavno mastektomijo
  - kontraindicirana je pri vnetnem raku dojk

MASTEKTOMIJA Z OHRANITVIJO KOLOBARJA IN BRADAVICE

- **Indikacije**
  - za mastektomijo z ohranitvijo kolobarja in bradavice se odločimo, če opravimo istočasno rekonstrukcijo dojke, sicer so indikacije enake kot za enostavno mastektomijo
  - **kontraindicirana je pri:**
    - → vnetnem raku dojk
    - → klinično prizadetem kompleksu kolobarja in bradavice
    - → oddaljenosti mamografsko, UZ ali MRI vidnih sprememb manj kot 1 cm od kompleksa kolobarja in bradavice
    - → krvavem izcedku iz bradavice



National Comprehensive Cancer Network

NCCN Guidelines Version 3.2015
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

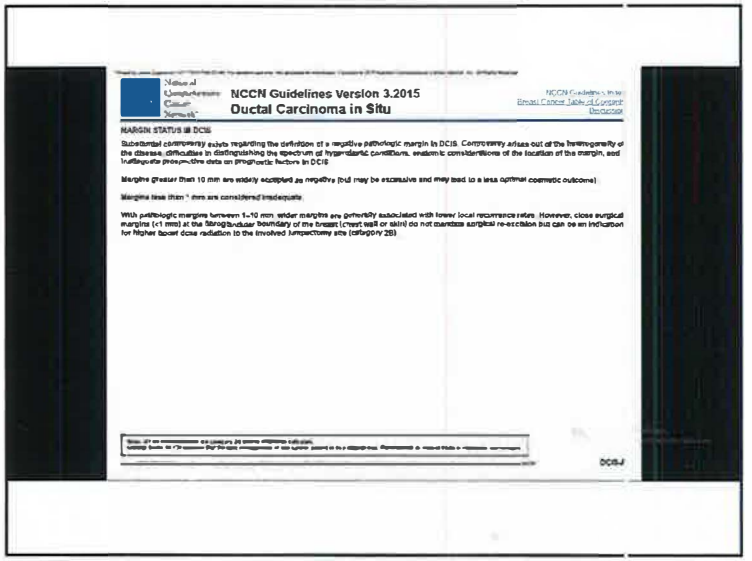
SPECIAL CONSIDERATIONS TO BREAST-CONSERVING THERAPY REQUIRING RADIATION THERAPY

Contraindications for breast-conserving therapy requiring radiation therapy include:

Absolute:
- Radiation therapy during pregnancy
- Diffuse suspicious or malignant-appearing microcalcifications
- Widespread disease that cannot be encompassed by local excision through a single incision that achieves negative margins with a satisfactory cosmetic result
- Positive pathologic margin[1]

Relative:
- Prior radiation therapy to the chest wall or breast; [illegible] is essential.
- Active connective tissue disease involving the skin (especially scleroderma and lupus)
- Tumors >5 cm (category 2B)
- Diffusely positive pathologic margins[1]
- Women with a known or suspected genetic predisposition to breast cancer:
  - May have an increased risk of ipsilateral breast recurrence or contralateral breast cancer with breast-conserving therapy
  - Prophylactic bilateral mastectomy for risk reduction may be considered

BINV-G



NCCN Guidelines Version 3.2015
Ductal Carcinoma in Situ

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

MARGIN STATUS in DCIS

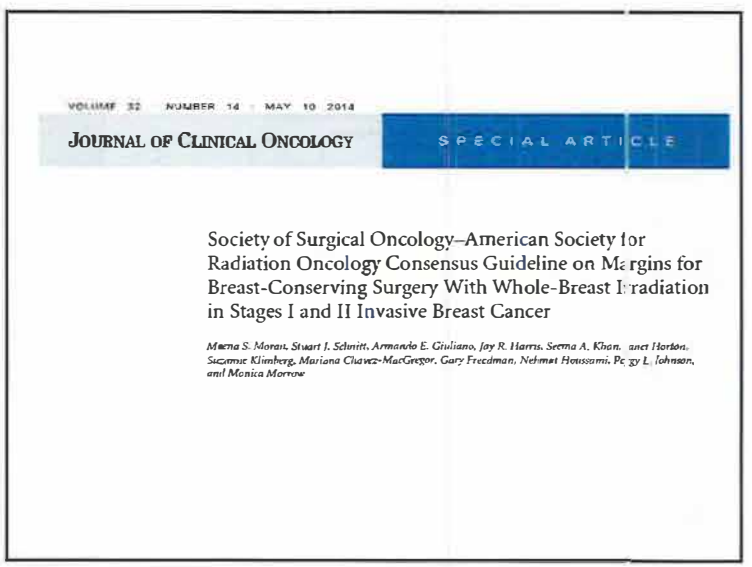
Substantial controversy exists regarding the definition of a negative pathologic margin in DCIS. Controversy arises out of the heterogeneity of the disease, difficulties in distinguishing the spectrum of hyperplastic conditions, anatomic considerations of the location of the margin, and inadequate prospective data on prognostic factors in DCIS

Margins greater than 10 mm are widely accepted as negative (but may be excessive and may lead to a less optimal cosmetic outcome)

Margins less than * mm are considered inadequate

With pathologic margins between 1–10 mm, wider margins are generally associated with lower local recurrence rates. However, close surgical margins (<1 mm) at the fibroglandular boundary of the breast (chest wall or skin) do not mandate surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site (category 2B)

DCIS-J



VOLUME 32 · NUMBER 14 · MAY 10 2014

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Society of Surgical Oncology–American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer

Meena S. Moran, Stuart J. Schnitt, Armando E. Giuliano, Jay R. Harris, Seema A. Khan, Janet Horton, Suzanne Klimberg, Mariana Chavez-MacGregor, Gary Freedman, Nehmat Houssami, Peggy L. Johnson, and Monica Morrow

Annals of Oncology Advance Access published May 4, 2015

Tailoring therapies - improving the management of early breast cancer: St GallenInternational Expert Consensus on the Primary Therapy of Early Breast Cancer 2015.

surgery of the primary

The Panel strongly endorsed recent findings that the minimal acceptable surgical margin was 'no ink on invasive tumour or DCIS'.

This conclusion applies regardless of tumour characteristics such as lobular histology, extensive intraductal component, young age, multifocality or multicentricity and unfavourable biological subtype [7].

A clear majority of the Panel agreed that multifocal and multicentric tumours could be treated with breast conservation, provided the above margin clearance was obtained and whole breast radiotherapy was planned.

Following neoadjuvant chemotherapy, the Panel did not consider it necessary to resect the entire area of the original primary if down-staging had occurred.

Table 1. Summary of Clinical Practice Guideline Recommendations

Clinical Question	Recommendation	Level of Evidence
What is the absolute increase in risk of IBTR with a positive margin? Can the use of radiation boost, systemic therapy, or favorable tumor biology mitigate this increased risk?	Positive margins, defined as ink on invasive cancer or DCIS, are associated with a two-fold increase in IBTR; the increased risk in IBTR is not nullified by delivery of a boost, delivery of systemic therapy (endocrine therapy, chemotherapy, biologic therapy), or favorable biology	Meta-analysis and secondary data from prospective trials and retrospective studies
Do margin widths wider than no ink on tumor cells reduce the risk of IBTR?	Negative margins (no ink on tumor) optimize IBTR; wider margin widths do not significantly lower this risk; the routine practice to obtain wide negative margin widths (more than no ink on tumor) is not indicated	Meta-analysis and retrospective studies
What are the effects of endocrine or biologically targeted therapy or systemic chemotherapy on IBTR? Should a patient who is not receiving any systemic treatment have wider margin widths?	Rates of IBTR are reduced with the use of systemic therapy; in the uncommon circumstance of a patient not receiving adjuvant systemic therapy, there is no evidence suggesting that margins wider than no ink on tumor are needed	Multiple randomized trials and meta-analysis
Should unfavorable biologic subtypes (such as triple-negative breast cancers) require wider margins (than no ink on tumor)?	Margins wider than no ink on tumor are not indicated based on biologic subtype	Multiple retrospective studies
Should margin width be taken into consideration when examining WBRT delivery techniques?	Choice of whole-breast radiation delivery technique, fractionation, and boost dose should not be dependent on margin width	Retrospective studies
Is the presence of LCIS at the margin an indication for re-excision? Do invasive lobular carcinomas require a wider margin (than no ink on tumor)? What is the significance of pleomorphic LCIS at the margin?	Wider negative margins than no ink on tumor are not indicated for invasive lobular cancer; classic LCIS at the margin is not an indication for re-excision; the significance of pleomorphic LCIS at the margin is uncertain	Retrospective studies
Should increased margin widths (wider than no ink on tumor) be considered for young patients (age < 40 years)?	Young age (< 40 years) is associated with both increased IBTR after BCT as well as increased local relapse on the chest wall after mastectomy and is also more frequently associated with adverse biologic and pathologic features; there is no evidence that increased margin width nullifies the increased risk of IBTR in young patients	Secondary data from prospective randomized trials and retrospective studies
What is the significance of an EIC in the tumor specimen, and how does this pertain to margin width?	EIC identifies patients who may have a large residual DCIS burden after lumpectomy; there is no evidence of an association between increased risk of IBTR when margins are negative	Retrospective studies

Abbreviations: BCT, breast-conserving therapy; DCIS, ductal carcinoma in situ; EIC, extensive intraductal component; IBTR, ipsilateral breast tumor recurrence; LCIS, lobular carcinoma in situ; WBRT, whole-breast radiation therapy.

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

First international consensus guidelines for breast cancer in young women (BCY1)

Ann H. Partridge[a,*], Olivia Pagani[b,c], Omaishiar Abulkhair[d], Stefan Aebi[e], Hédène Amant[f], Hatem A. Azim Jr.[g], Alberto Costa[h], Suzette Delaloge[i], Gloria Freilich[j], Oreste Davide Gentilini[k], Nadia Harbeck[l], Catherine M. Kelly[m], Sibylle Loibl[n,o], Oreste Marinow[p], Pedro Pereira[q,r], Bella Kaufman[s,t], Fátima Cardoso[u,v,w]

Table 4
Early breast cancer locoregional treatment.

Guideline statement	LoE
8. Surgical treatment of young patients with EBC – while being tailored to the individual patient – should in general not differ from that of older patients. Although, in general, young age is an independent risk factor for increased local recurrence after BCS and RT, it is also a risk factor for increased regional recurrence after mastectomy as well as systemic recurrence, thus conservative treatment does not seem to affect OS and the impact of side effects of more invasive loco-regional treatments is often higher.	I B I B

Breast Cancer Under Age 40: a Different Approach

D. Ribnikar, MD[1]
J. M. Ribeiro, MD[2]
D. Pinto, MD[2]
B. Sousa, MD[2]
A. C. Pinto, MD[2]
E. Gomes, MD[2]
E. C. Moser, MD, PhD[2]
M. J. Cardoso, MD[2]
F. Cardoso, MD, PhD[2,*]

Locoregional treatment

Surgery

Surgical treatment of BC in young women consisted, for many years, of mastectomy that was considered to be safer leading to less locoregional recurrences (LRR) and better OS. In the last decade, this concept was challenged with the results from large randomized trials in all age groups [32], and mastectomy even in young patients confers no OS advantage when compared to breast-conserving treatment (BCT) [33], followed by RT. Young age however remains as an independent risk factor for increased LRR after BCT [34] for both intraductal and invasive disease [35], despite the use of more effective adjuvant therapies [36]. Even considering the higher LRR in young women compared to other age groups, BCT if feasible should always be the preferred option [37]. The use of oncoplastic techniques is considered safe and seems particular useful when more extensive resections are needed. Young age is also a predictor of a gradual asymmetry between the treated and non-treated breast making oncoplastic techniques more important [38].

Breast Care

St. Gallen/Vienna 2015: A Brief Summary of the Consensus Discussion

Surgery of the Primary Tumor

Locoregional treatment aspects were again a major topic of this year's St. Gallen/Vienna Consensus: Despite extensive discussions, there were no major changes in technical aspects of primary tumor resection, but it can be noted the 'margin issue' appears now to be resolved and that oncoplastic techniques have found their role the field of breast-conserving surgery. Also, breast-conserving surgery was again confirmed as intended standard of care, also in cases of multifocal (72% Yes, 14% No, 14% Abstain) or multicentric (79% Yes, 21% No) disease, provided that clear margins can be achieved and whole-breast radiotherapy is planned.

When asked about the minimum acceptable surgical margin, 92% of panelists voted for 'no ink on invasive tumor', and 8% for '1–2 mm' clearance. The panel was clear on whether the margin required should depend on tumor biology (100% No), should be greater when age is less than 40 years (100% No), should be greater for lobular histology (100% No), and should be greater after neoadjuvant chemotherapy (90% No, 8% Yes, 2% Abstain). A clear majority of panelists felt that margins should not be greater in the presence of extensive intraductal component (80% No, 20% Yes) and greater for pure ductal carcinoma in situ than for invasive disease (80% No, 20% Yes).

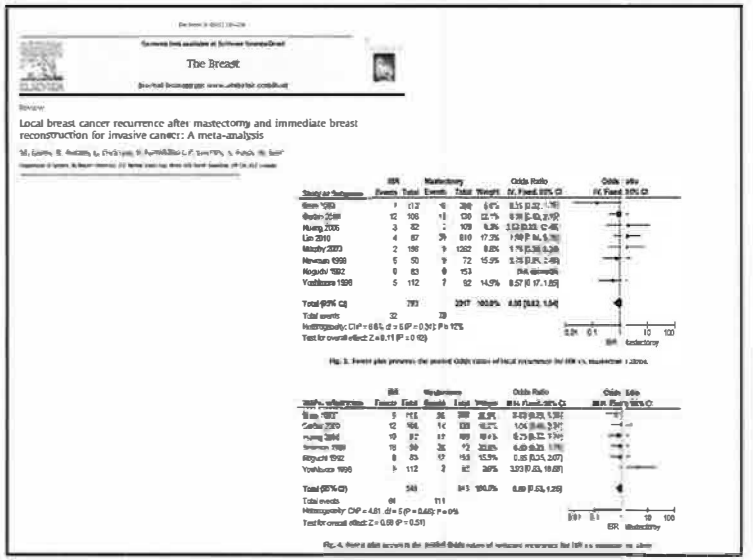
After downstaging by neoadjuvant chemotherapy, the entire area of the original primary does not need to be resected (89% Yes, 9% No, 2% Abstain).

Published in final edited form as:
Ann Surg. 2014 December ; 260(6): 1000–1010. doi:10.1097/SLA.0000000000000769

Contralateral Prophylactic Mastectomy after Unilateral Breast Cancer: A Systematic Review & Meta-Analysis

Oluwadamilola M. Fayanju, MD[1], Carolyn R. T. Stoll, MPH[2], Susan Fowler, MLIS[3], Graham A. Colditz, DrPH[2], and Julie A. Margenthaler, MD[1]

CPM. We recommend that UBC patients without known elevated FGR be advised against CPM, while patients with elevated FGR should be advised that while CPM would significantly decrease their risk of MCBC, it is unlikely to prolong their lives.



The Breast

Review

Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: A meta-analysis

Zaključek

- Delež mastektomij bi lahko/morali znižati
- K manj mastektomijam lahko pripomore
  - Nova spoznanja in smernice
  - Uvedba tehnik onkoplastične kirurgije
  - Več argumentiranega pogovora z bolnicami

Multidisciplinary team approach and onco-plastic surgery in Breast cancer treatment

Prof. **Uroš Ahčan,** MD, PhD
Consultant plastic, reconstructive and aesthetic surgeon
Department of Plastic Surgery & Burns
University Medical Center Ljubljana

Breast Cancer realities

- More than 350.000 breast cancer cases per year (EU)[1]
- **One in 10** women in the EU-27 will develop breast cancer
- **Most frequent** cancer type among women(~30%)[1]
- The incidence of breast cancer has been **increasing** for many years in economically developed countries.
- Over the thirty year period 1979-2008 the annual number of new cases of breast cancer in women almost **doubled**.

Sources:
[1] GLOBOCAN 2008 (International Agency for Research on Cancer) Web Site http://globocan.iarc.fr/
[2] Lee C, Belkora J, Chang Y, Moy B, Partridge A, Sepucha K, Are Patients Making High-Quality Decisions about Breast Reconstruction after Mastectomy? Plastic and Reconstructive Surgery, January 2011
[3] EUPHIX European Union Public Health Information System Breast cancer occurrence,
[4] *Eurostat*,
[5] Internal market assessment; Mentor Reconstruction Summit

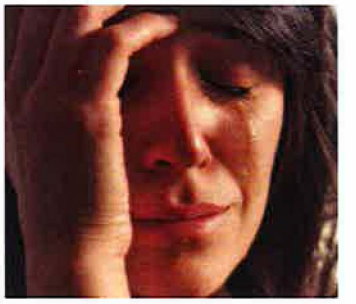
Breast Cancer realities

- 45% of BC patients are facing a mastectomy[4]
- ONLY **~20%** reconstruction rate[5]
- Very low level of awareness/information about breast cancer and reconstruction options[2] (**70%** of women who are eligible for the procedure are not well informed about their reconstructive)

Sources:
[1] GLOBOCAN 2008 (International Agency for Research on Cancer) Web Site http://globocan.iarc.fr/
[2] Lee C, Belkora J, Chang Y, Moy B, Partridge A, Sepucha K, Are Patients Making High-Quality Decisions about Breast Reconstruction after Mastectomy? Plastic and Reconstructive Surgery, January 2011
[3] EUPHIX European Union Public Health Information System Breast cancer occurrence,
[4] *Eurostat*,
[5] Internal market assessment; Mentor Reconstruction Summit

patient with breast cancer

What she needs?



Breast CA treatment strategy

What she needs?

- Proper information ("breast cancer" google=> 400.000.000 hits)
- Skilled surgeons (team)
- All possible methods of Ca Th & REC
- Best material (expanders & implants)
- Best pre & post operative care
- Psychological support

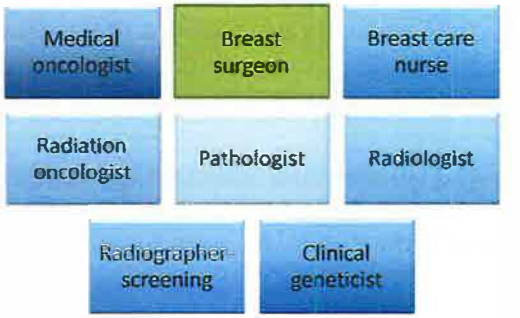
Modern treatment of breast cancer is multidisciplinary and multi-professional

2 Team approach in breast cancer care

LJUBLJANA experience
Functional Breast Unit

➢**Oncology core team**

Oncology core team



All team members should have basic knowledge on breast reconstruction options and procedures to deliver consistent information to the patient

Oncology core team

Profound knowledge

- Pathology of the disease
- Diagnostic procedures
- Multimodality treatments
  - Systemic treatment
  - Radiotherapy
  - Specific surgical procedures

Oncology core team

- establish the diagnosis (triple assessment),
- determine the stage of the disease,
- decide for surgical and (neo)adjuvant therapy.

Basic information about breast reconstruction – integral part of breast CA treatment

A key role in the treatment of breast cancer is played by the team of oncologists

Reconstructive core team

All team members should have basic knowledge on onco&plastic treatment to deliver consistent information to the patient

Other (optional) team members

Multi-disciplinary Case Management Meeting

Patient willing to undergo breast reconstruction

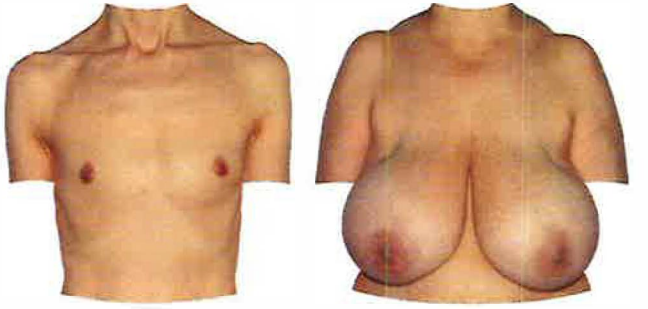
REC rate 60%

Multi-disciplinary Case Management Meetings (MDM)

Multidisciplinary team approach provide comprehensive assessment and consultation and the best possible treatment under specific circumstances.

breast reconstruction planning

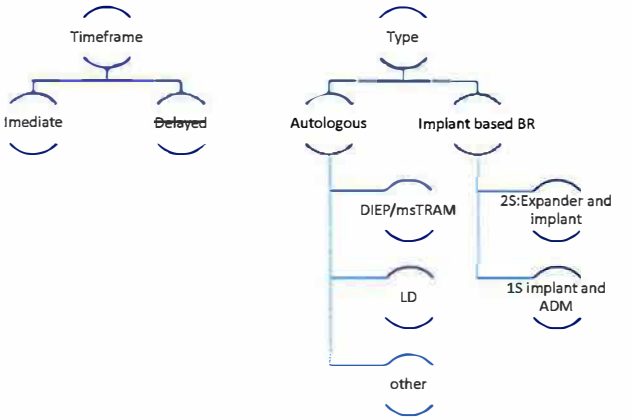
Assess relevant clinical factors influencing what to suggest to the patient



age, tissue quality and quantity, glandular characteristics, breast ptosis, pectoralis muscle characteristics...

scars, radiodermatitis, obesitas

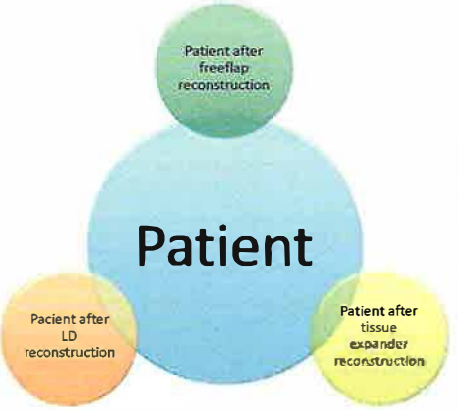
Reconstruction decision tree



Patient – subjective opinions

patient can talk with other women from Breast cancer support groups who have had mastectomies & reconstruction, about personal experience,

subjective feelings.

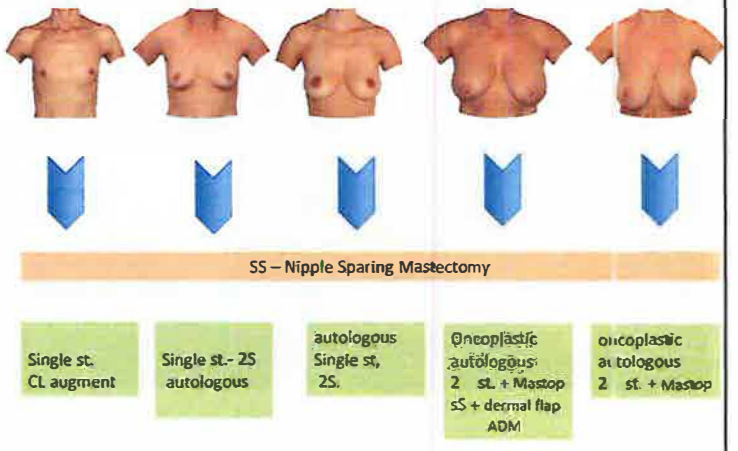


Breast cancer support group

Priceless support

The ultimate decision regarding the oncologic treatment and type of breast reconstruction is made by the patient after consultation!

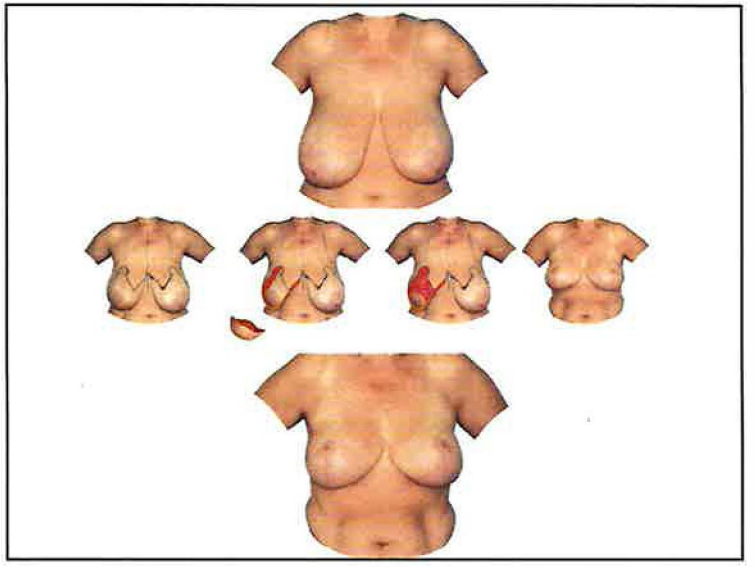
... oncoplastic surgery, breast reconstruction with implants, autologous tissue (flaps, lipografting), or combination of different methods



Teamwork forms the basis for modern breast cancer treatment and personalized approach

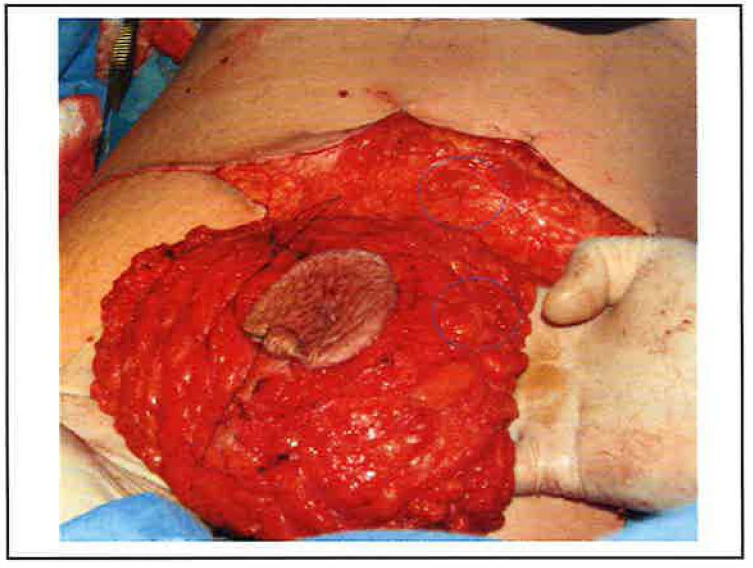
Reconstructive options

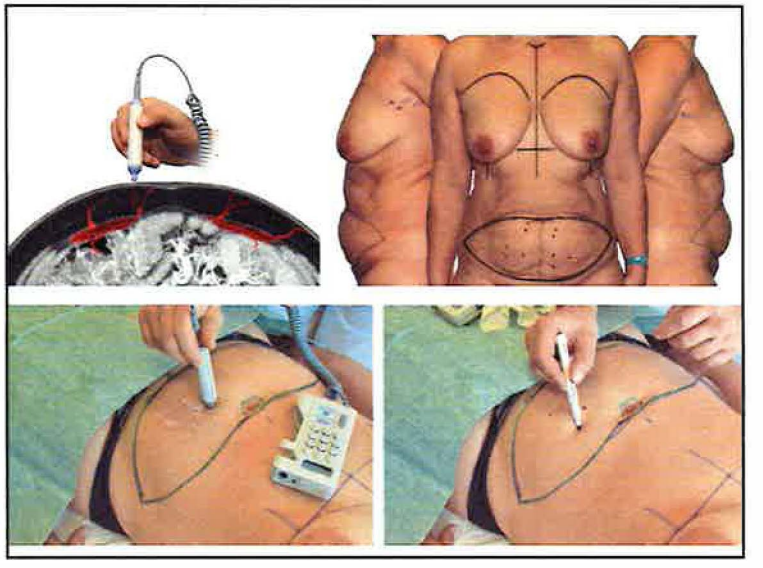
Oncoplastic surgery
Autolgous reconstruction
Implants based reconstruction
Combination

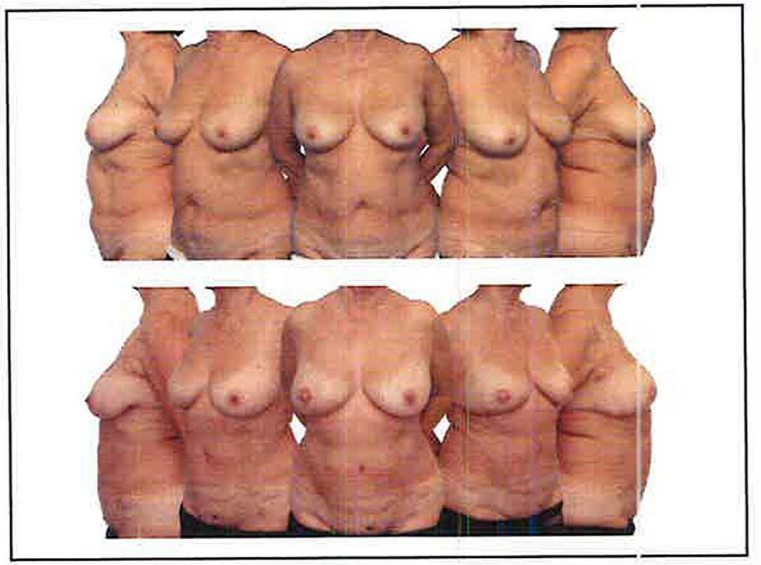


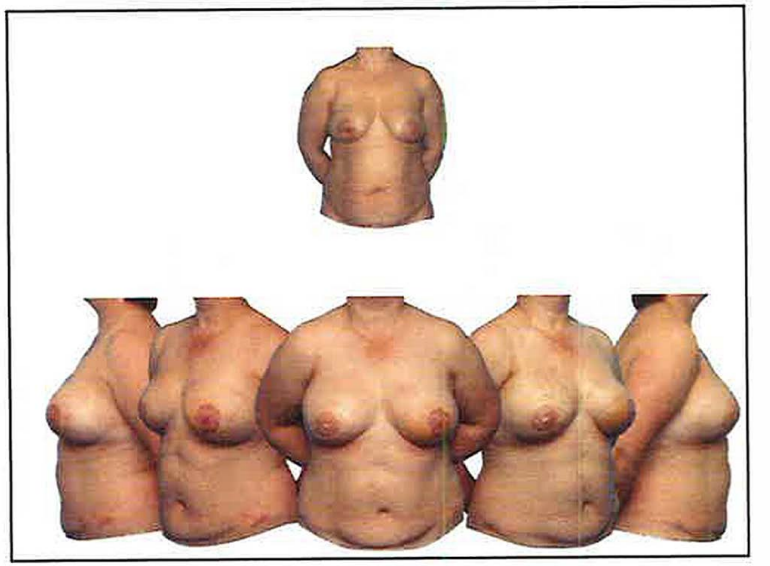
Reconstructive options

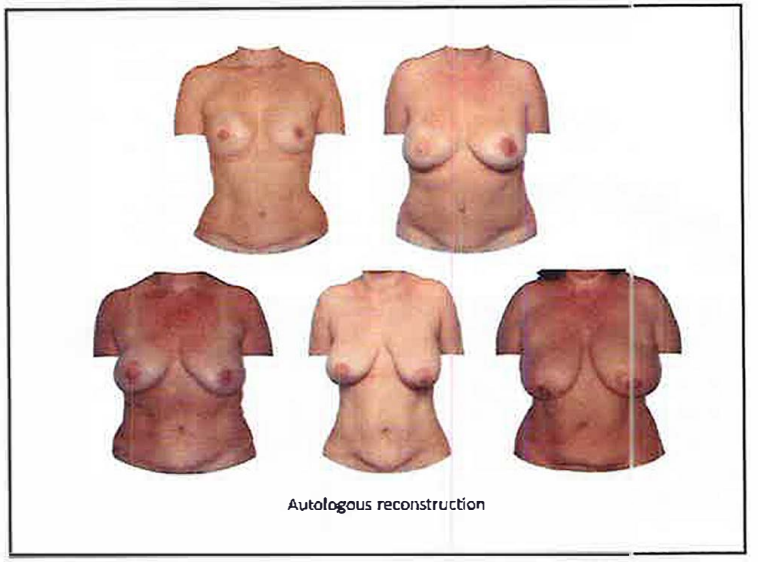
Oncoplastic surgery
Autolgous reconstruction
Implants based reconstruction
Combination



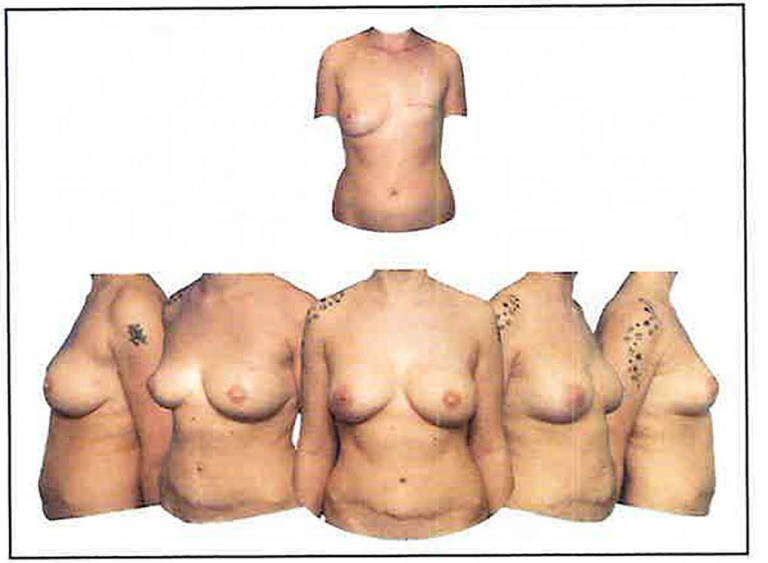


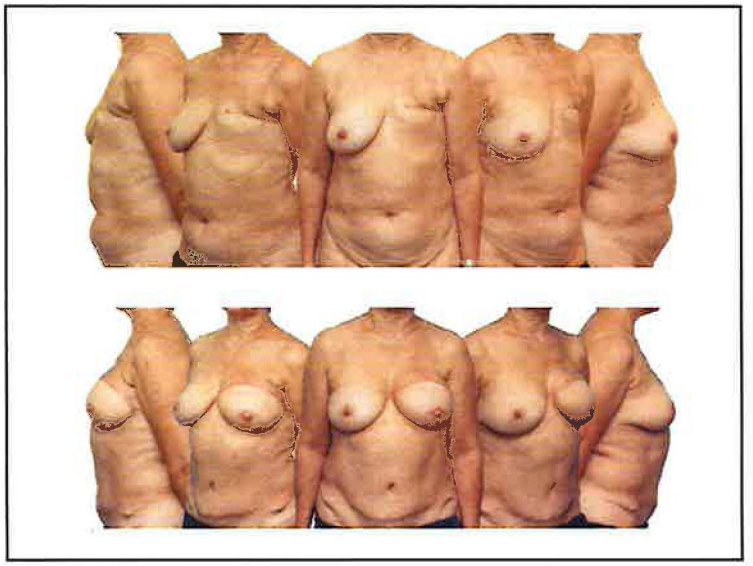


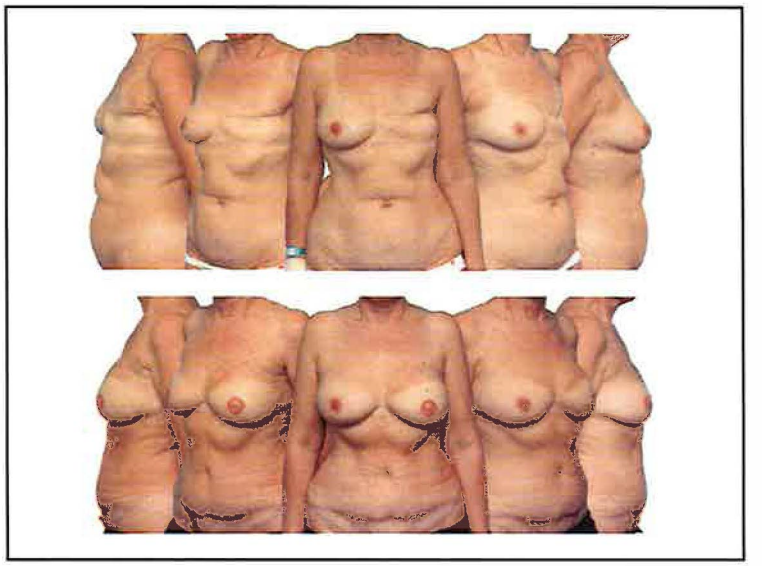


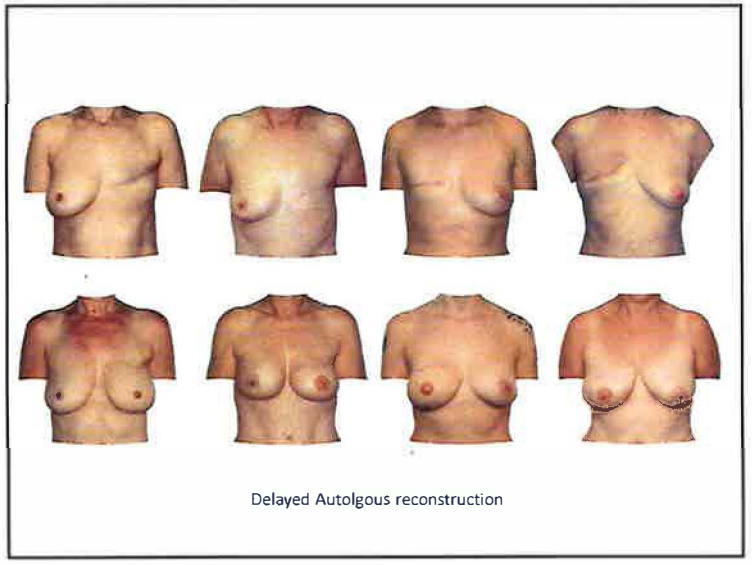


Autologous reconstruction

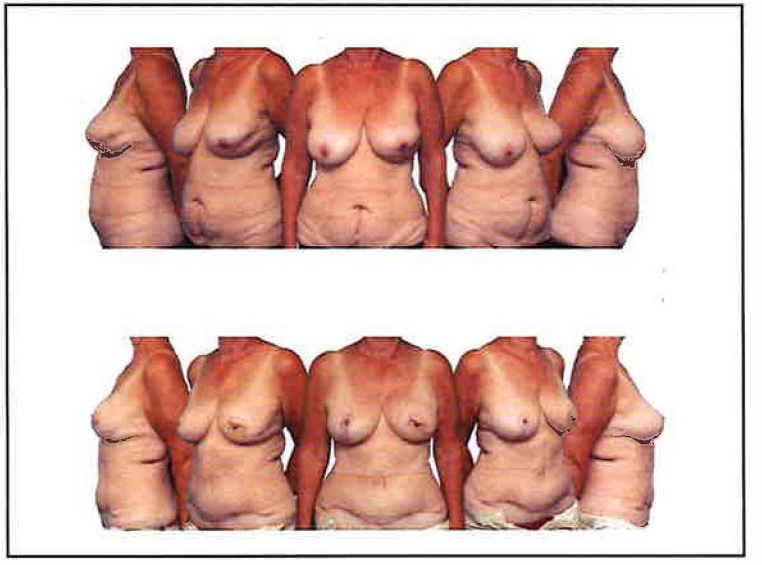


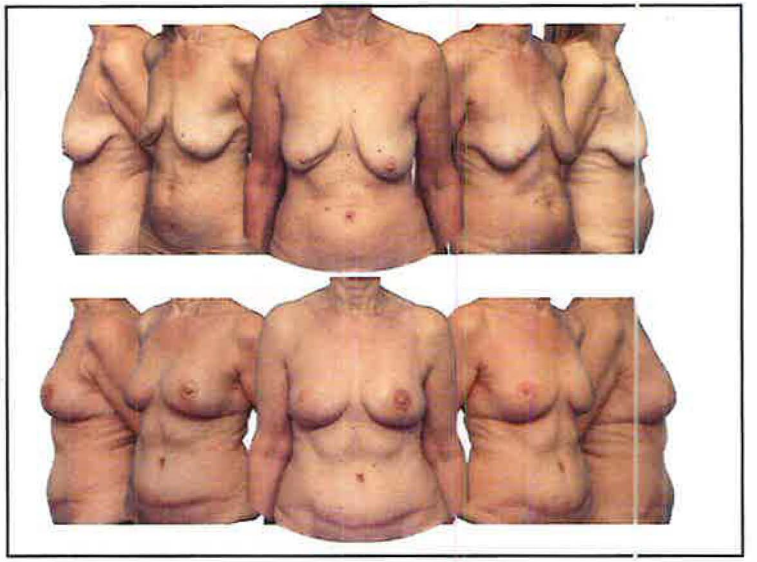






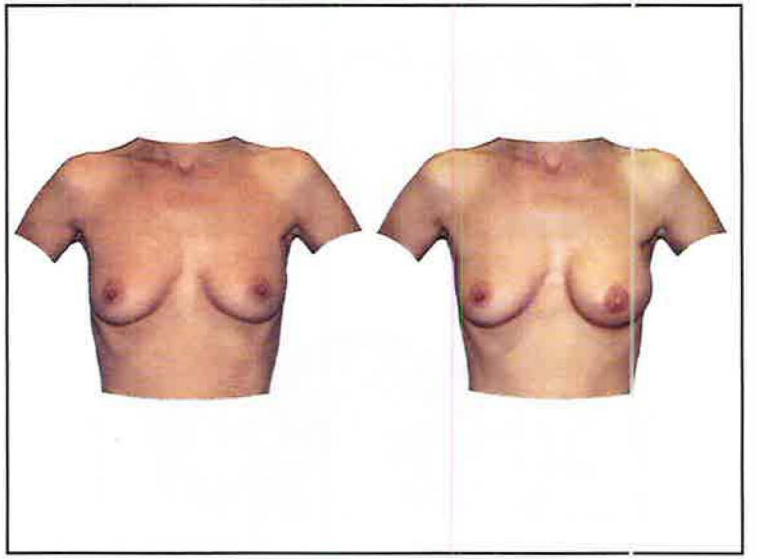
Delayed Autolgous reconstruction

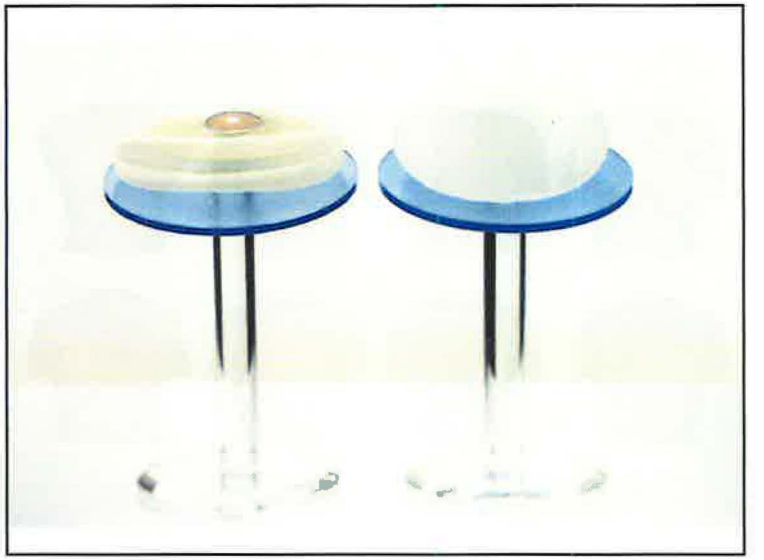




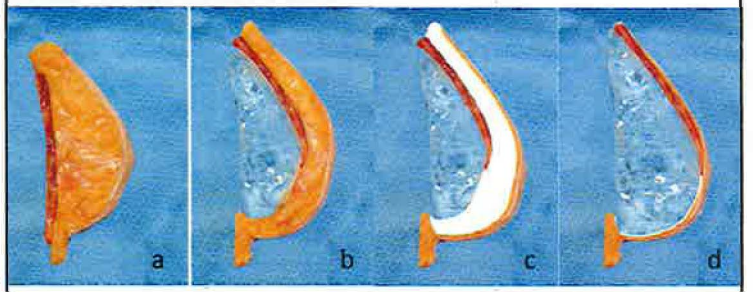
Reconstructive options

Oncoplastic surgery
Autolgous reconstruction
Implants based reconstruction
Combination

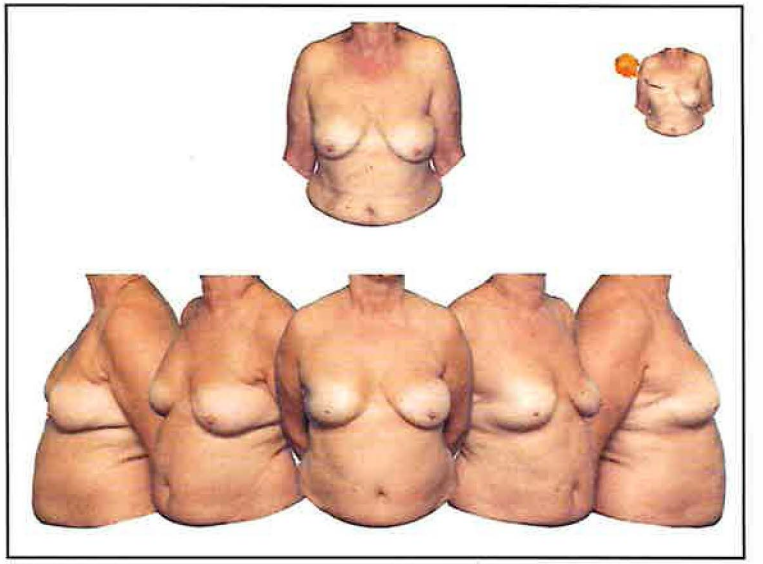


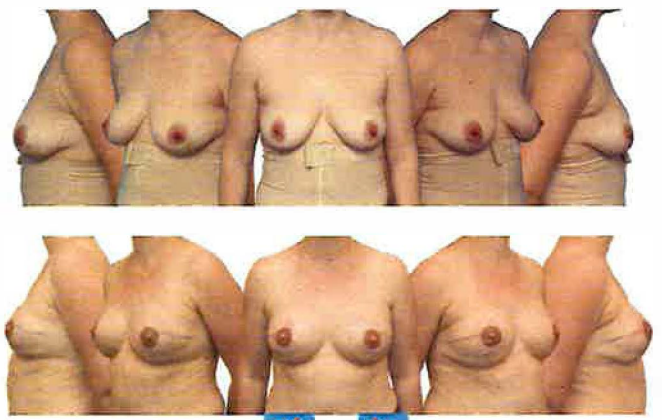


Preoperative measurements & appropriate implant selection



In comparison to breast augmentation (b), bigger implant with greater projection on the lower pole of the breast should be considered in IBBR (d).

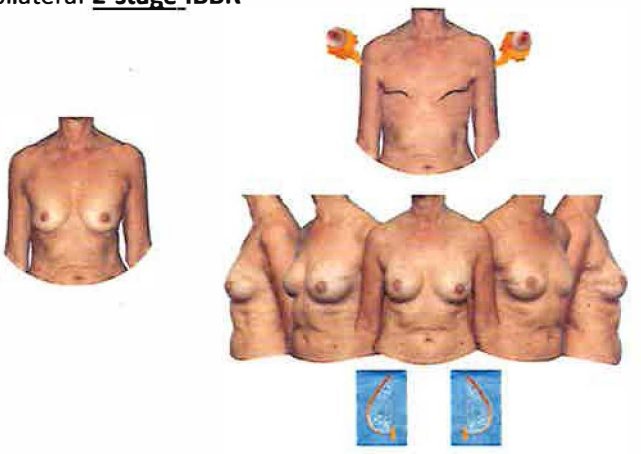




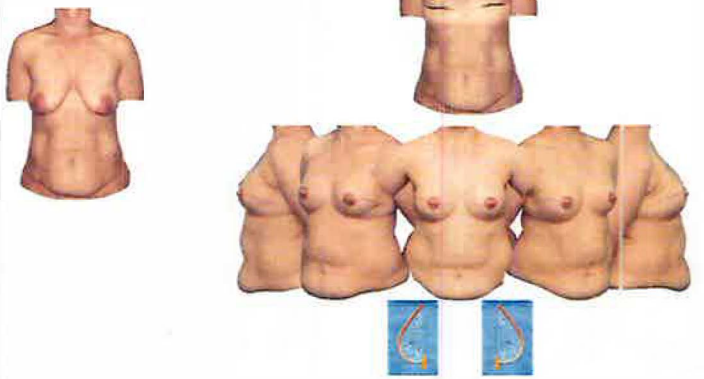
bilateral **2-stage IBBR**

Mentor CPG™ Implant 323, 495 cc 323, 495 cc

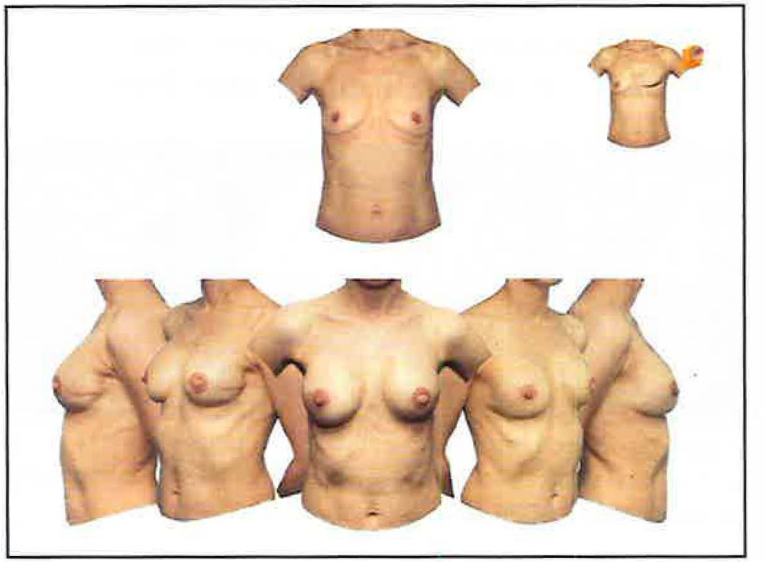
appropriate implant selection
in bilateral **2-stage IBBR**

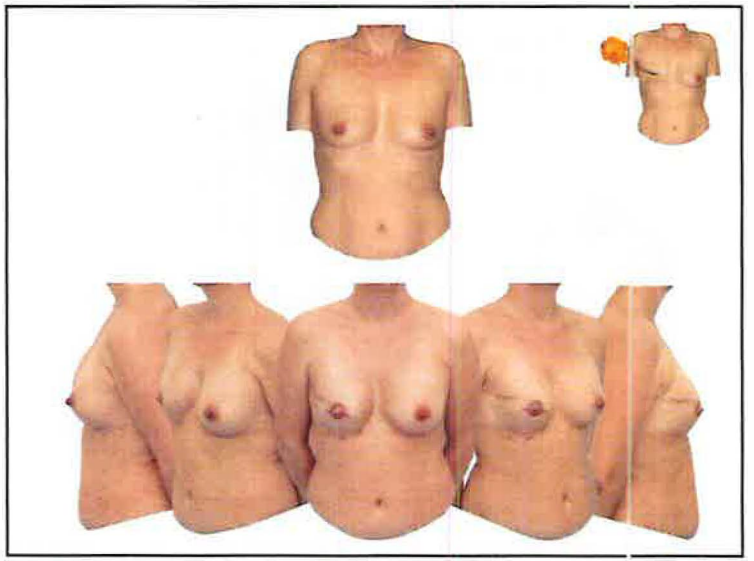


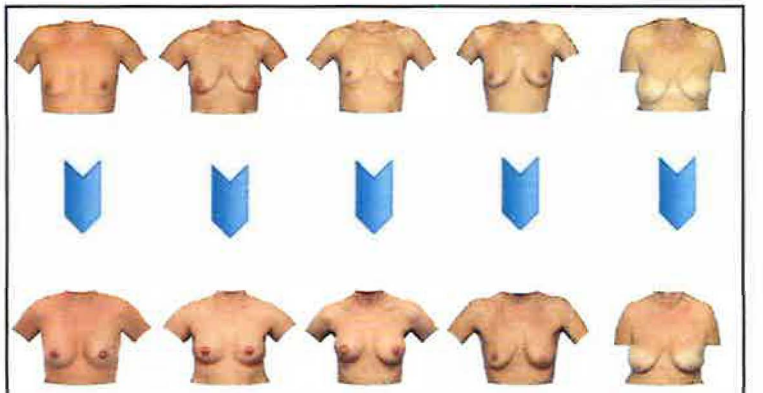
appropriate implant selection
in bilateral **2-stage IBBR**



Mentor CPG™ Implant 323, 495 cc 323, 495 cc



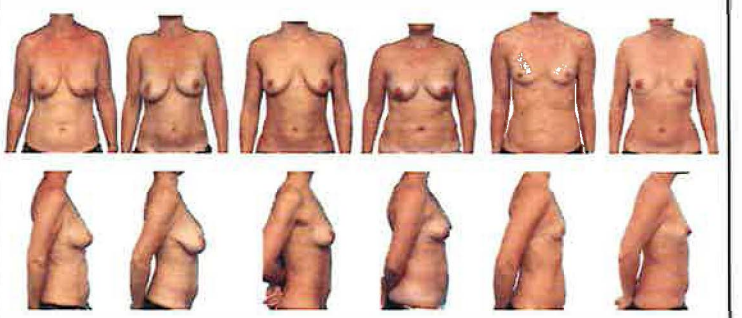




Even with implants we can recreate breasts of different sizes and shapes, even ptotic breasts with shorter post-operative recovery time, shorter hospital stay, no additional scaring and donor site morbidity.

New trends

- in the last decade the number of women with breast cancer having **bilateral mastectomy doubled** and more than **tripled** among women without breast cancer but with BRCA1/2 mutation or a high family risk **(high risk women)**.
- In USA rising trend in **CPM** (contralateral prophylactic mastectomy)



Studies showed that the average woman's age undergoing bilateral prophylactic mastectomies, varies from 38.1 – 40.7 years

(younger, fit patient, less invasive surgery, IBBR)

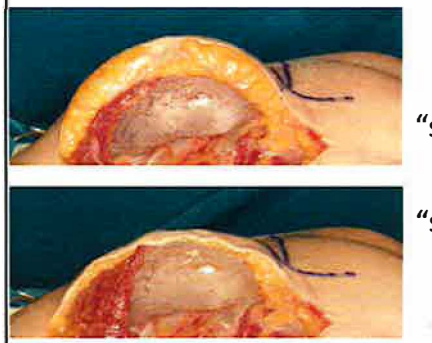
IMPLANTS based **BREAST RECONSTRUCTION**

IBBR is not just a "variation of breast augmentation".

With an experienced surgeon, breast augmentation is a simple and straightforward surgical procedure of a short duration and minimal complication rates.
However,
Tebbetts et al. described and categorised **53 variables** – that can influence the final result of every breast augmentation – in clinical, tissue and surgeons' factors

The main factor that needs to be taken into consideration in IBBR is the

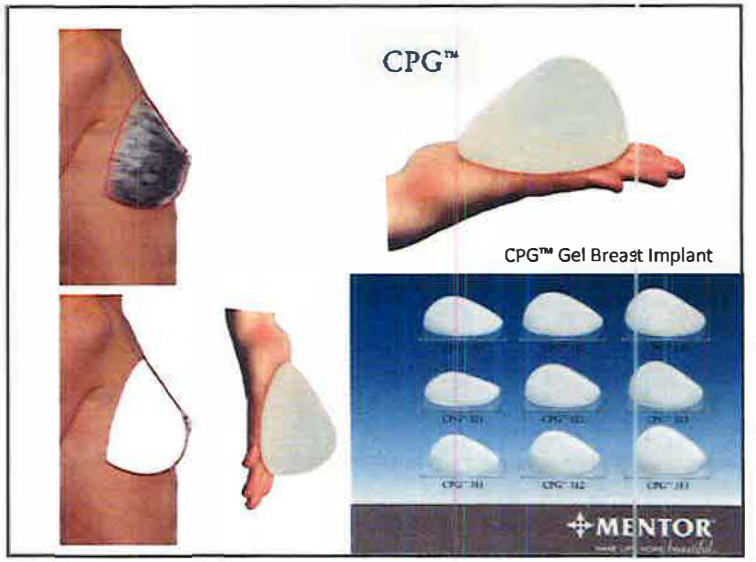
absence of breast tissue after SS or NS mastectomy



"soft tissue envelope"

"skin envelope"

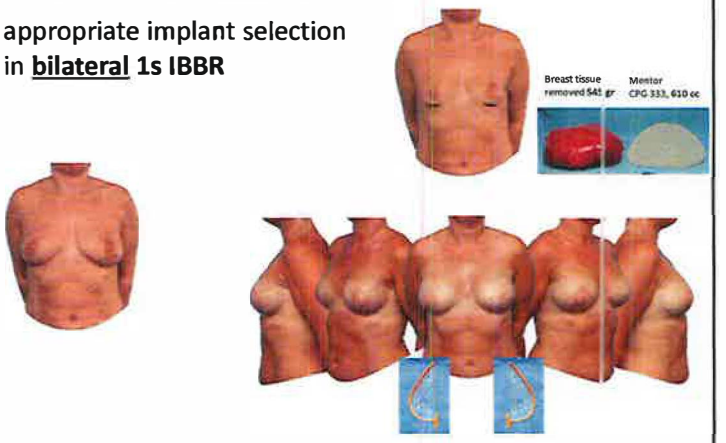
Comparison of soft tissue coverage between breast augmentation (a) and breast reconstruction with implants (b), where breast tissue is absent, thus irregular, thin skin envelope is covering pectoralis major muscle and implant



appropriate implant selection in **unilateral 1s IBBR**

The removed tissue is simply replaced with an anatomical implant of similar shape and volume

appropriate implant selection in **<u>bilateral</u> 1s IBBR**

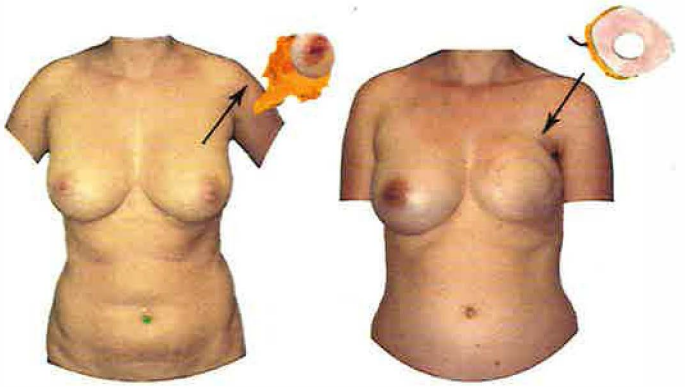


Result in 37 years old patient after bilateral NSM and single-stage reconstruction using anatomically shaped silicone implants (Mentor CPG™ Implant 333, 610 ml) & ADM.

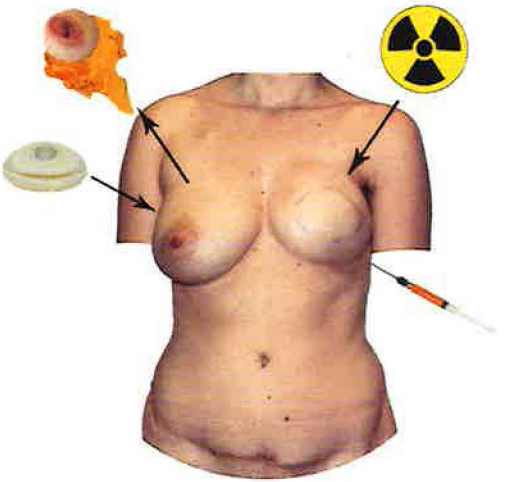
Reconstructive options

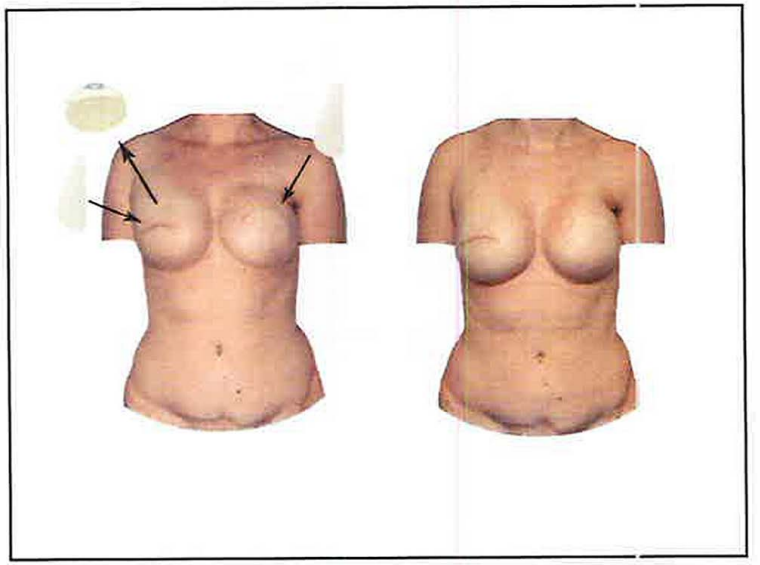
Oncoplastic surgery
Autolgous reconstruction
Implants based reconstruction
Combination

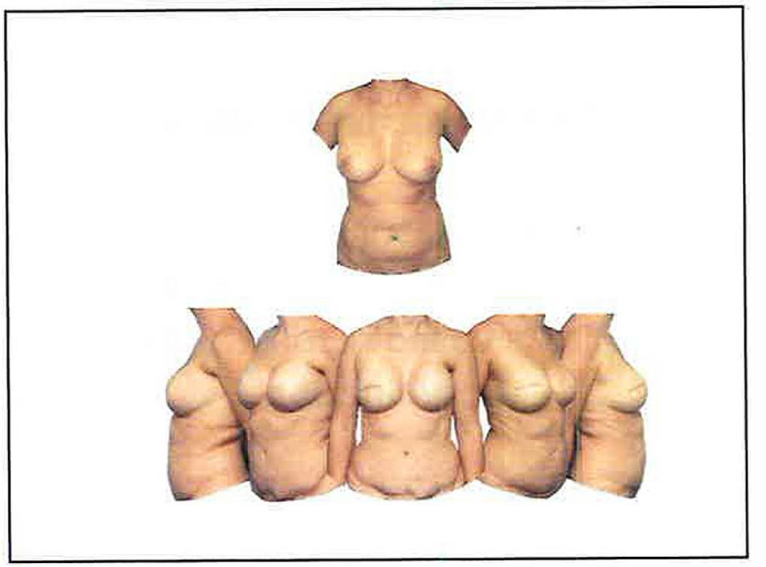
28 years old patient, left breast: invasive ductal CA



Immediate reconstruction with DIEP flap

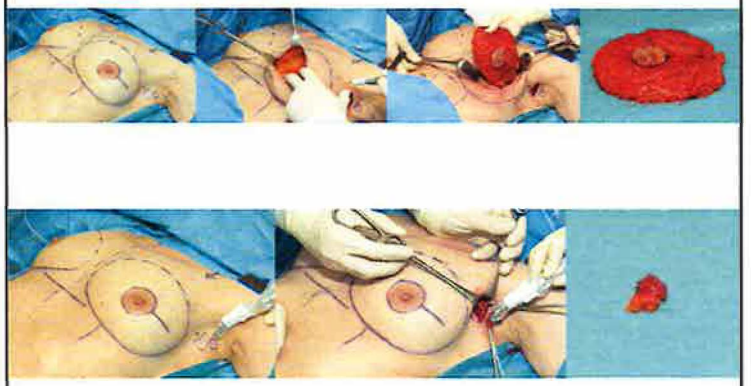







Team approach in OR


2 teams approach

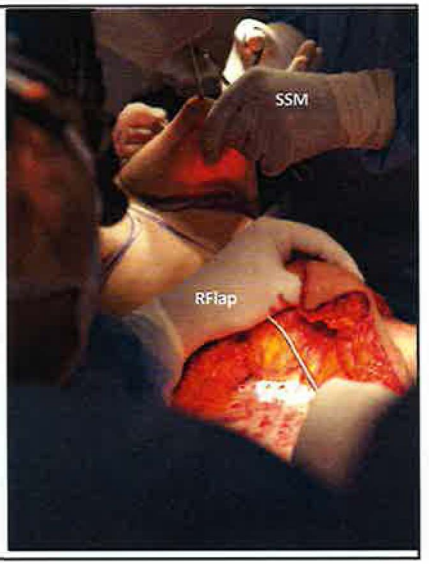


Breast surgeon: mastectomy, lymph node surgery, (SLB, axillary LND)

Benefit from 2-Team approach even in the OR

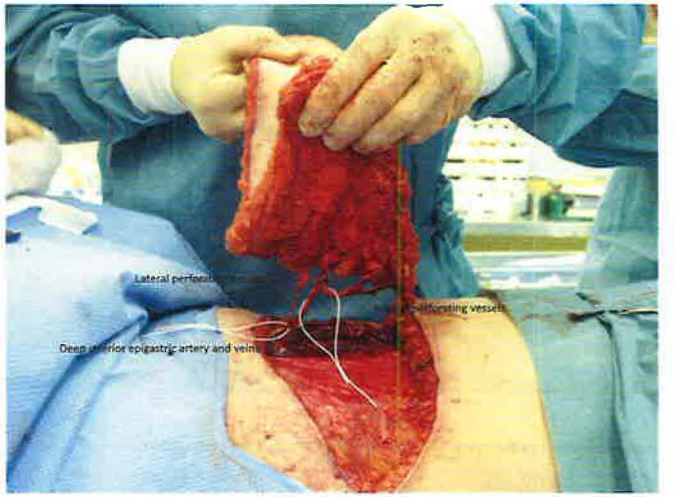
SSM
&
ms TRAM/DIEP
breast reconstruction

- Min 175 min (2,9 h)
- Max 435 min (7,25 h in billateral)
- Average 250 min **(4,1 h)**

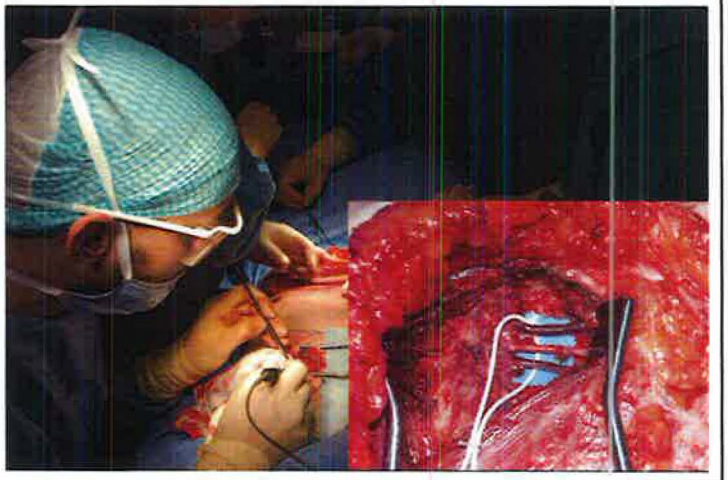


Delayed reconstruction

1 st team



2 nd team



UMC LJ in 2010, 2011, 2012

105 DIEPs	147 DIEPs	156 DIEPs
5 revision = 4,7%	6 revision = 4,1%	6 revision = 3,8 %
2 flaps lost = 1,9%	1 flaps lost = 0,7%	1 flaps lost= 0,6 %
98% successful rate	99,3% successful rate	99,4% successful rate

2013. 2014 100% successful rate

Consecutive series of **293** DIEP flaps without a flap failure

Treating Breast Cancer patients:

Is a "project" which should involve several parties – the patient herself, her husband & family and a group of medical professionals being her advisors.

If all of these parties work in a coordinated way and act with dedication and professionalism, the treatment can represent nothing more than an unpleasant transitional period from patient back to woman…

every woman deserves the right to choose the reconstruction option

Depending on country **reconstruction rate after mastectomy** is ~20% (0-40%)

Breast Reconstruction **integral** part **of breast cancer treatment**

to regain her natural breast shape and fullness… to restore life

optimization of autologous breast reconstruction **Ljubljana MC** part **1**

ms TRAM/DIEP flap
breast reconstruction

- Two team approach
- the use of reverse engineering technology
  - Additional team members - mechanical engineer

ms TRAM/DIEP breast reconstruction

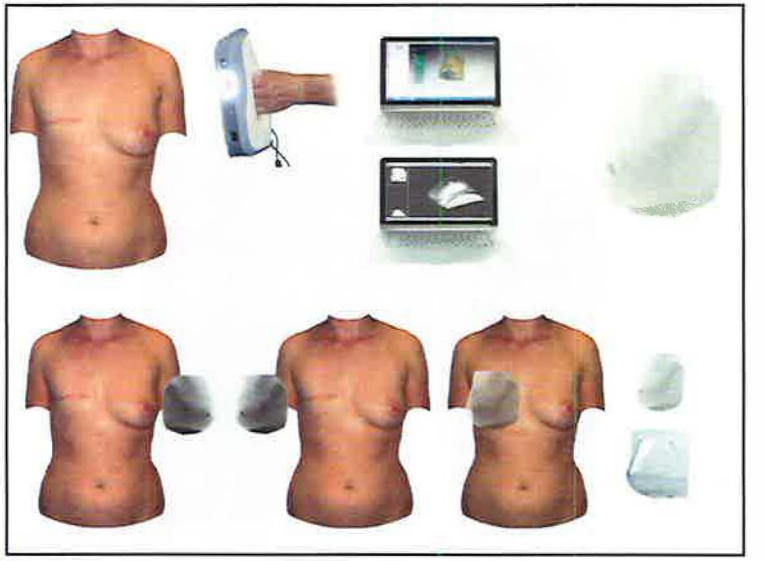
optimization of autologous 2nd breast reconstruction in Ljubljana MC

In order to achieve better breast symmetry in secondary breast recontruction where the footprint, conus, and skin envelope have been damaged dramatically, reverse engineering technology is used.

New technique

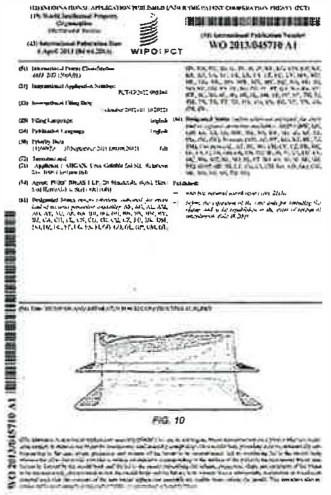
3D image of the remaining breast is taken according to the instruction from the plastic surgeon with 3D scanner by mechanical engineer.

Faculty of mechanical engineering



New technique

(healthy breast replica and a mold)



WIPO PCT

WO 2013/045710 A1

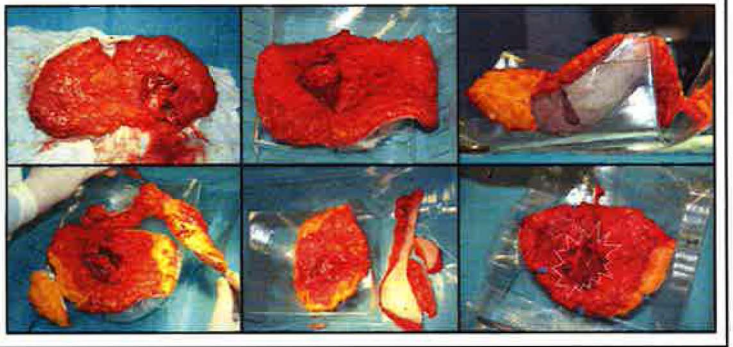
FIG. 10

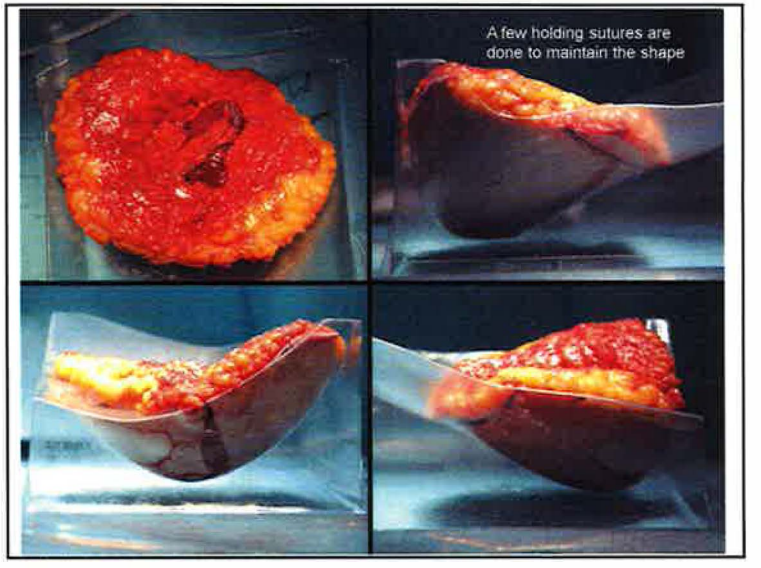
The mold has negative geometry of the contralateral breast and is used for tissue shaping during surgery.

optimization of shaping

Flap shaping in NBRC on the side table.

Excesive tissue is cut away. Perforators are maintained in the central part of new breast.

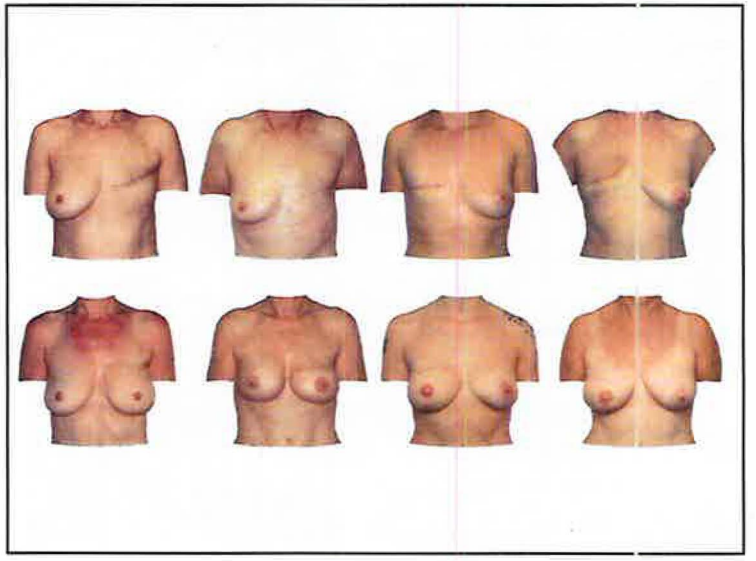




Transfer of the flap in the NBRC to the thoracic wall and microcurgery

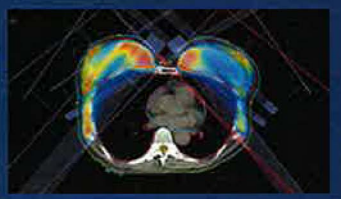
optimization of positioning

Positioning of the flap according to KSP (4+4) is done in few minutes with staples



Problem outline

Rekonstrukcija dojke in obsevanje



Tanja Marinko
Sektor radioterapije
Onkološki inštitut Ljubljana

Ljubljana, november 2015

Uvod

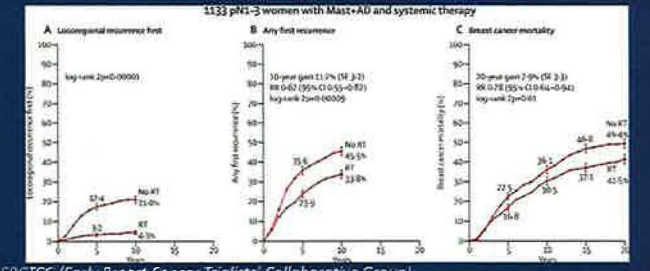
- 1. indikacije za obsevanje (RT) po mastektomiji
- 2. najprimernejši način rekonstrukcije dojke (RD) pri bolnicah, ki potrebujejo dopolnilno RT
- 3. dejavniki, ki vplivajo na končni izid zdravljenja z RT in RD

1. Indikacije za RT po mastektomiji

- tumor > 5 cm
- > 3 pozitivne bezgavke v pazduhi
- pozitivne parasternalne bezgavke
- ozki kirurški robovi oz. R1/R2 resekcija
- prizadeta koža (vnetni karcinom)
- če NAKT: RT glede na status pred začetkom zdravljenja
- Nova indikacija: 1 do 3 pozitivne bezgavke

1-3 pozitivne bezgavke

Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials



EBCTCG (Early Breast Cancer Trialists' Collaborative Group)
Lancet, vol 383, junij 2014

1-3 pozitivne bezgavke

- **Odprto vprašanje:**
  RT res potrebna pri vseh starostih in pri vseh bioloških podtipih? Pri vseh (enaka) dobrobit?
- Čakamo objavo napovedane analize, zaenkrat se odločamo individualno glede na starost bolnice in biološke lastnosti tumorja

2. Najprimernejši način rekonstrukcije

- **NCCN smernice (verzija 3. 2015):**
- pri predhodno obsevanih bolnicah je uporaba tkivnih razširjevalcev /vsadkov relativno kontraindicirana zaradi slabšega estetskega izida (večja možnost kapsularne kontrakture, malpozicije, ...). Priporočajo rekonstrukcijo z lastnim tkivom.
- Takojšnja rekonstrukcija je kontraindicirana pri vnetnem raku dojke- čimprejšnje obsevanje!

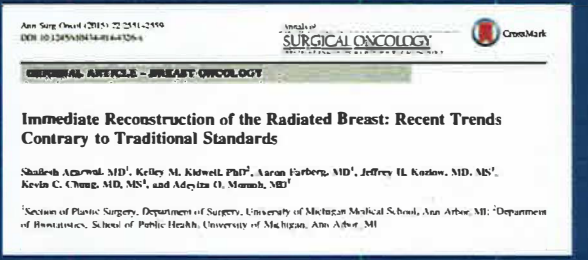
- **Če je načrtovana RD z lastnim tkivom in RT :**

Priporočajo odloženo rekonstrukcijo (po RT) ali pa takojšnjo RD s tkivnim razširjevalcem in po obsevanju RD z lastnim tkivom

- **Če je načrtovan vsadek in RT :**

Priporočajo takojšnjo RD s tkivnim razširjevalcem in po obsevanju (lahko pa tudi pred njim) trajni vsadek.

Takojšnja vstavitev trajnega vsadka ni priporočljiva, če je predvidena RT (več zapletov).


Ann Surg Oncol (2015) 22:2551–2559
DOI 10.1245/s10434-015-4564-x

Annals of SURGICAL ONCOLOGY

CrossMark

ORIGINAL ARTICLE – BREAST ONCOLOGY

Immediate Reconstruction of the Radiated Breast: Recent Trends Contrary to Traditional Standards

Shailesh Agarwal, MD[1], Kelley M. Kidwell, PhD[2], Aaron Farberg, MD[1], Jeffrey H. Kozlow, MD, MS[1], Kevin C. Chung, MD, MS[1], and Adeyiza O. Momoh, MD[1]

[1]Section of Plastic Surgery, Department of Surgery, University of Michigan Medical School, Ann Arbor, MI; [2]Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, MI

ABSTRACT

Background. Immediate, implant-only breast reconstruction is traditionally discouraged in patients who receive radiation. It is not clear whether this widely recognized mantra of breast reconstruction is observed in practice. The purpose of this study was to evaluate immediate reconstruction trends and practices in patients who have undergone mastectomy and radiation therapy.

Conclusions. The frequency of immediate reconstruction continues to increase in the setting of postmastectomy radiation therapy, with immediate implant-based reconstruction representing the most commonly utilized method, contrary to traditional recommendations. These findings likely reflect changing attitudes towards implant reconstruction in the setting of planned postmastectomy radiation.

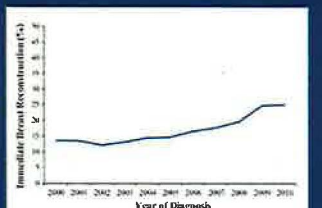
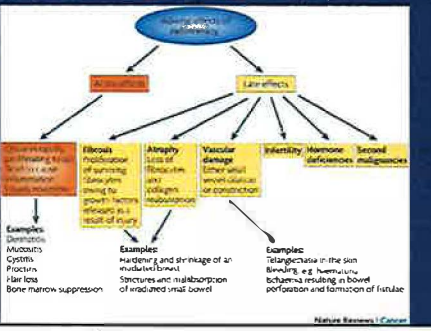


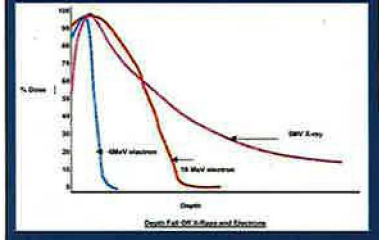
FIG. 1 Immediate breast reconstruction rate from 2000 to 2010 in patients requiring radiation (6,875 reconstructions/40,568 women with breast cancer)

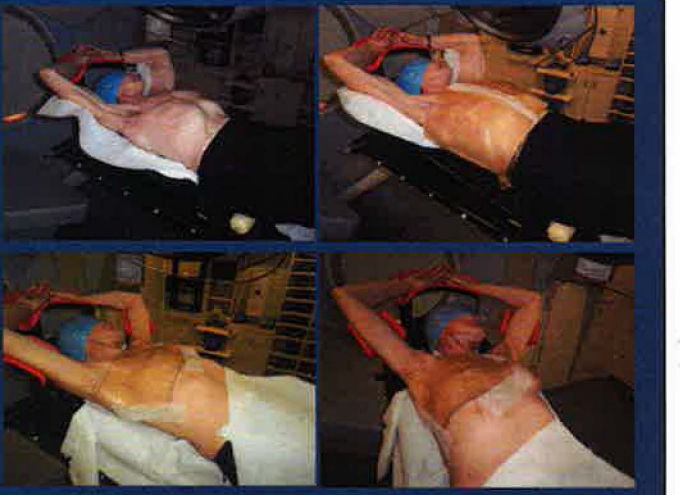
3. Dejavniki, ki vplivajo na končni izid zdravljenja z RT in rekonstrukcijo dojke

- kasne posledice zdravljenja z obsevanjem
  (vpliv prejete sistemske terapije in lastnosti posameznika)

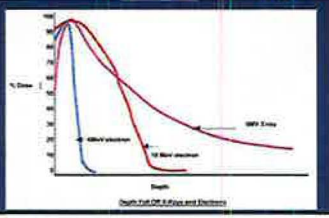


1. Bolus - uporabimo pri ozkih sprednjih robovih





I. Bolus – uporabimo tudi če je tarčno tkivo nad vsadkom zelo tanko, da zagotovimo pokritost s predpisano dozo



- **Velikost bolusa odvisna od tega, kako natančno lahko opredelimo, kje je bil problematičen rob (najbolje, če so na tem mestu klipi...)**

Primer :

- Bolnica LHM, ablacija in takojšnja rekonstrukcija z lastnim tkivom

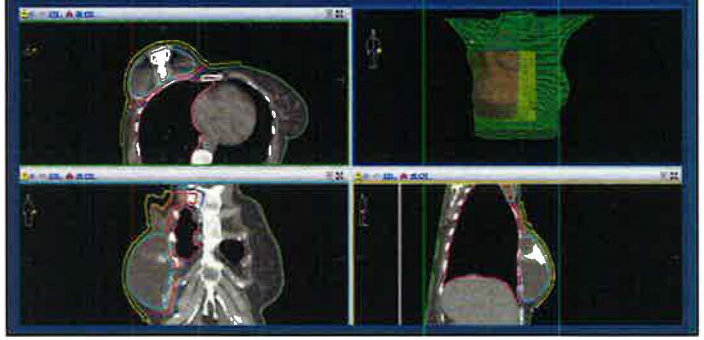
- HI: DCIS, velik 2,5 cm, v zun. zg. kvadr., sr. in visoki gradus, tu celice v bližini ant.roba (v območju vidnega polja velike povečave)

Primer :

Bolnica KR, MRM s takojšnjo rekonstrukcijo (tkivni razširjevalec)

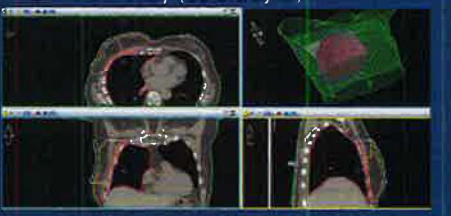
- RT: zaradi tanke prsne stene bolus na desno dojko

PTV1 : TD= 25 x 2 Gy

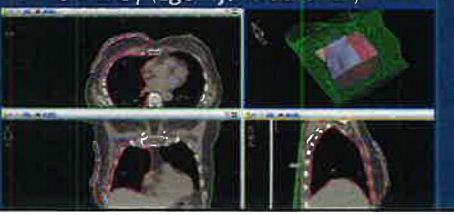


- RT: bolus čez zunanji zgornji kvadrant

PTV 1: TD = 25 x 2 Gy (cela dojka)



PTV 2: TD = 5 x 2 Gy (zgornja kvadranta)



II. dodatek doze na ležišče tumorja:

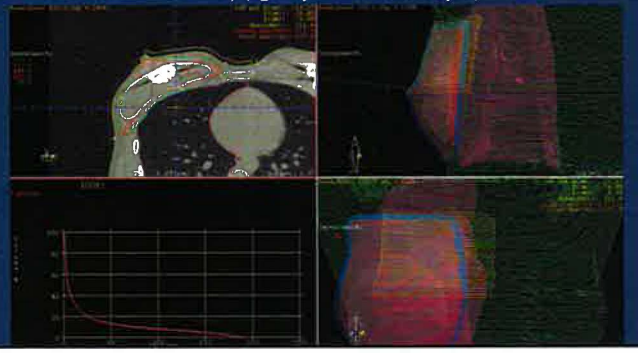
- predpišemo pri ozkih ali pozitivnih robovih
- če ni jasno, kje je problematičen rob, potem obsevamo celo mamarno regijo (rekonstruiranmo dojko) z višjo dozo
- skupna prejeta doza: TD= (30-33) X 2 Gy = 60-66 Gy
- posledično slabši estetski izid zdravljenja !

Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

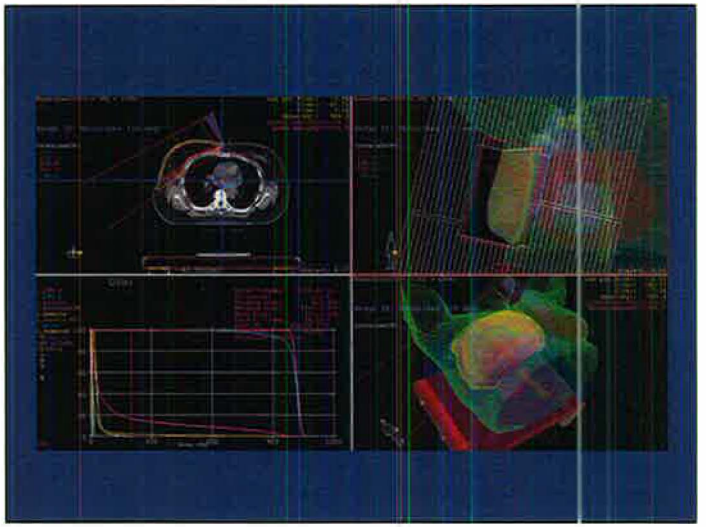
Bartelink H, Lancet Oncology, vol 16, januar 2015

- **Bolnice:** maj 1989- junij 1996
- **Metode:**
  - mikroskopsko kompletna odstranitev invazivnega Ca dojke
  - Pooperativna RT: 25 x 2 Gy
  - randomizacija:
    brez boosta (2657 bolnic) /16 Gy boosta (2661 bolnic)
  - Srednji čas opazovanja: 17.2 let
- **Rezultati:** dodatek boosta izboljša lokalno kontrolo (HR 0,65)
- (ne vpliva pa na preživetje) vendar poslabša estetski izid:
- **Kumulativna incidenca izrazite fibroze po 20 letih :**
  1,8 % (brez boosta) / 5,2% (boost) (p< 0.001)

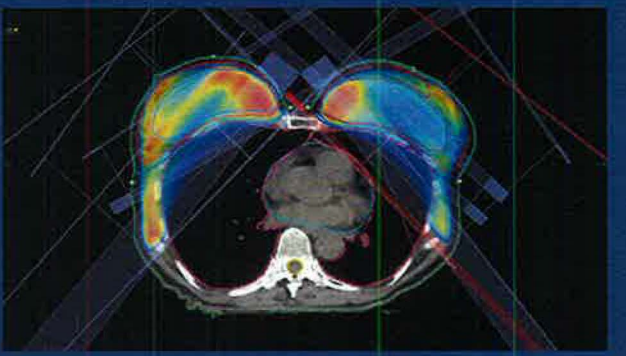
Primer : Bolnica DD; mastektomija s takojšnjo rekonstrukcijo (tkivni razširjevalec), IDC in DCIS; DCIS blizu sprednjega roba (v območju vidnega polja velike povečave)
RT: - bolus na zgornjem notranjem kvadrantu
- PTV1: TD=25 x 2Gy (cela dojka)
- PTV 2: TD= 5 x 2 Gy (zgornja kvadranta dojke)



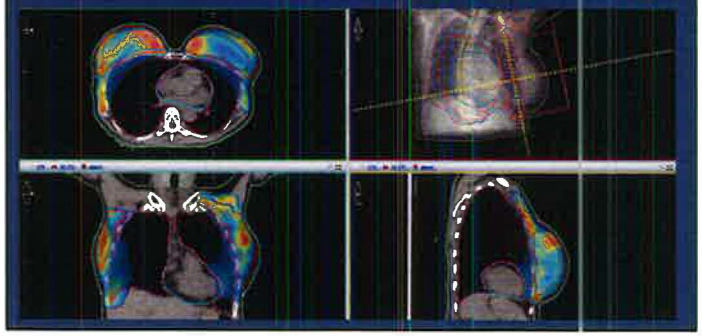
- **Primer:**
- Bolnica MN ; MRM s takojšnjo rekonstrukcijo z lastnim tkivom, dodatna ekscizija tkiva dojke:
- HI: multipla žarišča IDC blizu (v območju vidnega polja velike povečave) kavtersko poškodovanega roba (tkivo iz podkožja)
- RT : bolus čez celo rekonstruirano dojko
  - PTV 1: dojka + scl, TD = 25 x 2 Gy
  - PTV 2: dojka, TD = 5 x 2 Gy



- polnjenje tkivnega razširjevalca : NE, vse od priprave na simulatorju dalje pa do konca obsevanja, ker izdelan obsevalni načrt sicer ne ustreza več!



- delno praznjenje vsadka zaradi (boljše) izvedljivosti RT:
- če je začasni vsadek zelo napolnjen, je zelo težko pripraviti optimalen obsevalni načrt - za bolnico bolje, če ga delno izpraznimo – pred pripravo na simulatorju !



zaključek

- ne glede na vrsto rekonstrukcije, na končni estetski izid zdravljenja z operacijo in RT vplivajo še drugi dejavniki, ki jih je potrebno upoštevati: npr. bolus, dodatek doze zaradi tesnih robov
- Pri bolnicah z 1-3 pozitivnimi bezgavkami po mastektomiji z RT podaljšamo preživetje

Novosti v predoperativnem sistemskem zdravljenju raka dojk

Simona Borštnar
Oddelek za internistično onkologijo
Onkološki inštitut Ljubljana

19. oktober 2015

- Namen predoperativnega sistemskega zdravljenja
- Definicija patološkega popolnega odgovora
- Patološki popolni odgovor kot nadomestni cilj kliničnih raziskav
- Novosti v predoperativnem zdravljenju trojno negativnih rakov
- Novosti v predoperativnem zdravljenju HER2 pozitivnih rakov

Namen predoperativnega sistemskega zdravljenja

Namen predoperativnega sistemskega zdravljenja

- Vpliv na kirurško zdravljenje:
  - Zveča operabilnost in delež ohranitvenih operacij[1]
  - Zmanjša zaplete operativnega zdravljenja [2]
  - Zmanjša potrebo po kirurški reoperaciji zaradi rezidualnega tumorja[3]
- Učinku prilagojeno zdravljenje:
  - Prekinitev/sprememba neuspešnega predoperativnega zdravljenja
- Napoved izhoda bolezni glede na odgovor (patološka remisija)
  - Patološka popolna remisija napoveduje dober izhod bolezni[4]
- Hitrejši prenos spoznanj iz kliničnih raziskav
  - Patološka kompletna remisija kot nadomestni pokazatelj uspešnosti zdravljenja namesto DFS in OS?

1. Kaufmann, *et al. Ann Surg Oncol* 2012;
2. Abi, *et al. JAMA Surg* 2014;
3. Jeevan, *et al. BMJ* 2012;
4. Cortazar *et al. Lancet* 2014

Definicija patološkega popolnega odgovora

Definicija patološkega popolnega odgovora

Patološki popolni odgovor kot nadomestni cilj kliničnih raziskav

Zakaj je predoperativno sistemsko zdravljenje pomembno za ovrednotenje učinka novih terapij

Prednosti raziskav v predoperativnem zdravljenju v primerjavi z dopolnilnim:
- Hiter razvoj dogodka (krajše trajanje raziskav)
- Možnost translacijskih raziskav (primerjava lastnosti tumorja pred in po sistemski terapiji)
- Potrebno manjše število bolnikov

Guidance for Industry

Pathological Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, rm. 2201
Silver Spring, MD 20993-0002
Ed. 301-796-3400, Fax: 301-847-8714, E-mail: druginfo@cder.fda.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2014

VI. IMPLEMENTATION OF THE GUIDANCE

Since the release of the draft version of this guidance in May 2012, the FDA has participated in public discussions regarding this pathway for drug development. In March 2013, the FDA and the American Society of Clinical Oncology co-sponsored a public neoadjuvant breast cancer workshop with an expert panel of breast cancer experts seeking to discuss the use of pCR to support accelerated approval.[8] The panel concluded that a large improvement in pCR rate based upon analysis of a full intent-to-treat population was reasonably likely to predict clinical benefit, and that the potential advantages of granting accelerated approval based upon pCR from a neoadjuvant randomized controlled trial generally outweighed concerns. The panel emphasized that such trials should be limited to high-risk patients, and that a confirmatory trial should be ongoing at the time of accelerated approval.

Združena analiza 12 kliničnih raziskav predoperativne KT (N=11955)

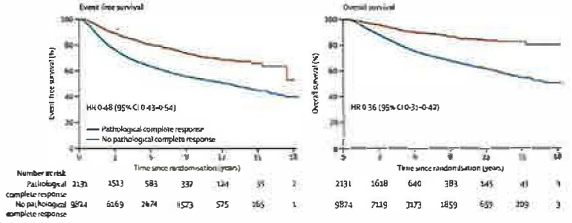
Namen raziskave:

- ugotoviti povezavo med patološkim popolnim odgovorom in časom brez ponovitve bolezni ter celotnim preživetjem,
- razpoznati ustrezno definicijo patološkega popolnega odgovora, ki najboljše korelira z izhodom bolezni,
- razpoznati podtipe, pri katerih patološkim popolnim odgovorom najboljše korelira z izhodom bolezni in
- ugotoviti ali večji delež patološkim popolnim odgovorom napoveduje izboljšanje preživetja brez napredovanja bolezni (EFS) in celotnega preživetja (OS)

1. Untch M, *et al. J Clin Oncol* 2009; 27:2938–2945. 2. von Minckwitz G, *et al. J Clin Oncol* 2005; 23:2676–2685. 3. Untch M, *et al. Ann Oncol* 2011; **22**:1999–2006. 4. Bonnefoi H, *et al. Lancet Oncol* 2011; 12:527–539. 5. von Minckwitz G, *et al. Ann Oncol* 2005; 16:56–63. 6. von Minckwitz G, *et al. J Natl Cancer Inst* 2008; 100:552–562. 7. Bear HD, *et al. J Clin Oncol* 2006; 24:2019–2027. 8. Wolmark N, *et al. J Natl Cancer Inst Monogr* 2001; 30:96–102. 9. Gianni L, *et al. J Clin Oncol* 2009; 27:2474–2481. 10. Gianni L, *et al. Lancet Oncol* 2014; 15:640–647. 11. Untch M, *et al. J Clin Oncol* 2011; **29**:3351–3357. 12. von Minckwitz G, *et al. J Clin Oncol* 2010; **28**:2015–2023.

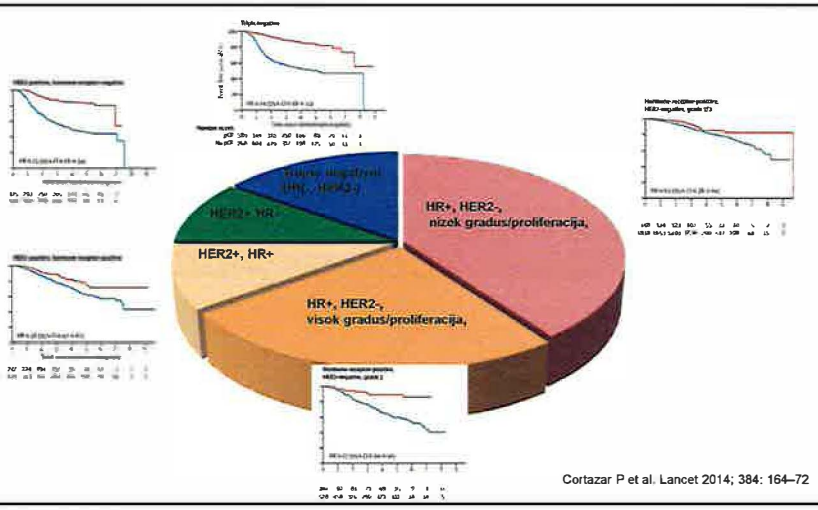
Cortazar P et al. Lancet 2014; 384: 164–72

Povezava med tpCR ter EFS in OS



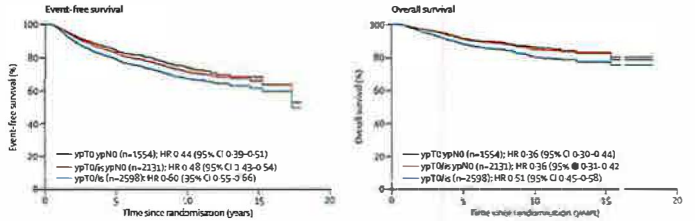
tp CR= odsotnost invazivnega raka v dojki in pazdušnih bezgavkah po predoperativni KT
EFS= čas brez napredovanja bolezni (izhodišče opazovanja je randomizacija, dogodek je lokalno napredovanje bolezni ali oddaljeni zasevki ali smrt iz kateregakoli razloga
OS= celotno preživetje (izhodišče je randomizacija, dogodek je smrt)

Cortazar P et al. Lancet 2014; 384: 164–72



Cortazar P et al. Lancet 2014; 384: 164–72

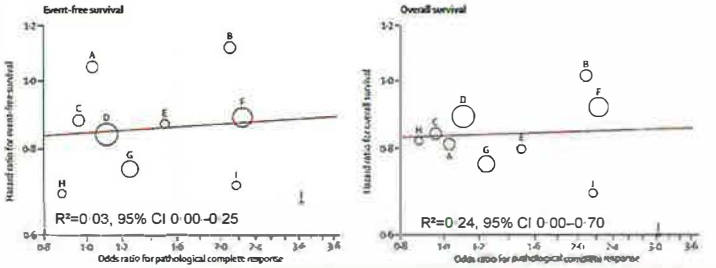
Katera definicija popolnega patološkega odgovora najboljše napoveduje izhod bolezni



ypT0ypN0= odsotnost invazivnega raka in in situ raka v dojki in pazdušnih bezgavkah
ypT0/isYpN0= odsotnost invazivnega raka v dojki in pazdušnih bezgavkah (ne glede na DCIS)
ypT0/is= odsotnost invazivnega raka v dojki (ne glede na DCIS in infiltracijo pazdušnih bezgavk)

Cortazar P et al. La cet 2014; 384: 164–72

Korelacija med deležem bolnikov s pCR in izhodom bolezni



Možni razlogi zakaj delež pCR ni koreliral z izhodom bolezni:
- heterogena populacija
- majhen delež pCR pri HR+
- Majhen delež bolnic zdravljenih s tarčno terapijo
- del bolnikov je prejel tudi adjuvantno terapijo

Cortazar P et al. Lancet 2014; 384: 164–72

Novosti v predoperativnem zdravljenju trojno negativnih rakov

Soli platine v predoperativnem zdravljenju (randomizirane raziskave)

Study	No	Backbone Regimen	No Carbo	Carboplatin	p
GeparSixto	315	Tedenski paklitaksel+ liposomalni Doxo+bevacuzimab+/- tedenski karboplatin (AUC 1.5-2x 18)	38%	59%	<0.05
CALB 40603	433	Tedenski paklitaksel+/-bevacizumab +/-karboplastin (AUC 6) na 3 tedne x 4, nato ddACx 4	41%	54%	0.0029
Tamura et al	75	Tedenski paklitaksel +/-karboplastin (AUC 5) na 3 tedne x 4, nato CEF	26%	62%	
Alba et al	94	EC90 nato docetaksel +/- karboplatin (AUC 6) na 3 tedne x 4,	30%	30%	NS
Ando et al	75	Tedenski paklitaksel +/-karboplastin (AUC 5) na 3 tedne x 4, nato CEF x 4	26%	61%	0.0003

Von Minckwitz G et al, Lancet Oncology 2014, Sikov WM et al, JCO 20·5, Alba et al, Breast Cancer Res Treat 2012; Tamura K et al JCO 2014, Ando M et al . Breast Cancer Res Treat 2014

Meta-analiza predoperativne terapije s solmi platine pri trojno negativnem raku dojk (TNBC)

28 kliničnih raziskav (6 randomiziranih kliničnih raziskav,22 prospektivnih in retrospektivnih raziskav) N= 1598

	pCR
TNBC	
Skupni delež pCR s solmi platine	45%
KT s solmi platine vs. KT brez soli platine	HR=1.45
TNBC vs. ostali	
Zdravljeni s KT s solmi platine	HR 3.0

Petrelli F et al. Breast Cancer Res Treat 2014;144(2):223-232.

Povezava med mutacijo BRCA in odgovorom na predoperativno KT s cisplatinom

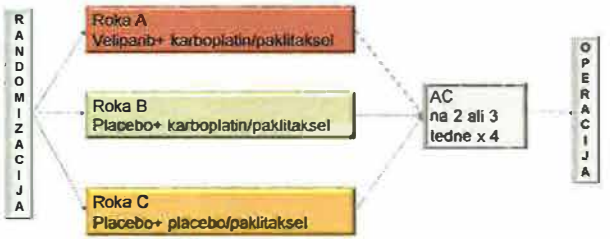
Avtor	Značilnost tumorja	Shema	N	pCR
Byrski	BRCA1 mutacija	KT brez soli platine	90	14(16%)
	BRCA1mutacija	Cisplatin75 mg/m2 x 4	107	65 (61%)
Silver	brez BRCA mutacije	Cisplatin75 mg/m2 x 4	26	4 (15%)
	BRCA 1 mutacija	Cisplatin75 mg/m2 x 4	2	2 (100%)
Ryan	Brez BRCA mutacije	Cisplatin75 mg/m2 x 4 + Bevacizumab 15 mg/kg x3	51	8 (16%)

Byrski T, et al. JCO 2009; 28(3):375-379; Byrski T, et al. Breast Cacer Res Treat 2014; 147 (2):401-5; Silver DF, et al. JCO 2010; 28(7):1145-53, Ryan PD, et al JCO 2009 ; 27(15S)

Zaviralci PARP pri trojno negativnem raku dojk (TNBC) (Raziskava BrighTNess; n=624)

TNBC
Stadij :T2-4 N0-2 ali T1N1-2

Stratifikacija:
BRCAstatus;
N0 vs 1-2
AC na 2 ali 3 tedne



Primarni cilj raziskave: pCR

Veliparib: 2x 50mg po 12 tednov; karboplatin: AUC 6 iv a 3 tedne x 4; paklitaksel 80mg/m² tedensko x 12, AC:doksorubicin 60 mg/m² /ciklofosfamid 600 mg/m²

Trenutna priporočila izbora predoperativne KT za HER2 negativne rake

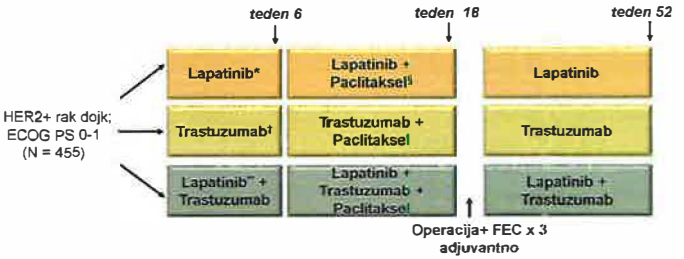
- Kemoterapija z antraciklini in taksani v sosledju (npr):
  - FEC na 3 tedne 3-4x→ $DOCE_{100}$ na 3 tedne 3-4x
  - FA(E)C na 3 tedne 3x -→ $Paklitaksel_{80}$ tedensko x 12
  - AC_{DD} x 4 na 2 tedna 4x-→ $Paklitaksel_{80}$ tedensko x 12
  - AC_{DD} x 4 na 2 tedna 4x→ $Paklitaksel_{175}$ na 2 tedna x 4
- Soli platine (še) niso vključene v trenutna priporočila

KT NAJ BO ZAKLJUČENA PRED OPERACIJO !

Novosti v predoperativnem zdravljenju HER2 pozitivnih rakov

NeoALTTO/BIG 1-06: Predoperativna terapija s lapatinibom in/ali trastuzumabom

► Randomizirana, multicentrična, odprta klinična raziskava faze III



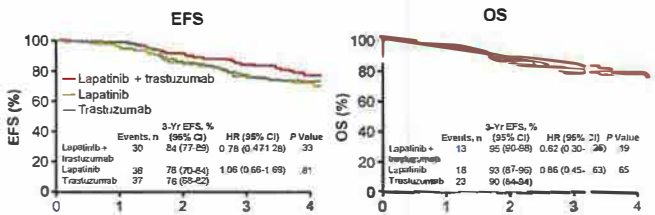
*lapatinib 1500 mg/dan; trastuzumab 4 mg/kg, nato 2 mg/kg tedensko; ‡lapatinib 1000 mg/dan, znižan odmerek na 750 mg/dan s paclitakselom, paclitaksel 80 mg/m²/teden.

Baselga J, et al. Lancet 2012;379:633-640.

NeoALTTO: rezultati

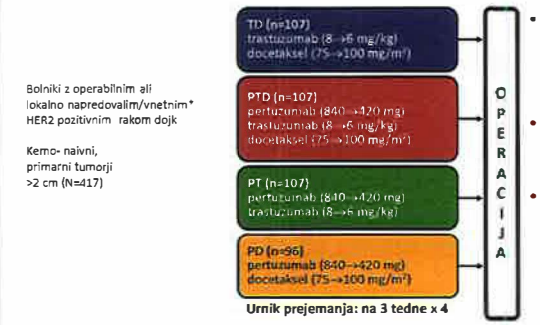
► Večji delež pCR pri dvojni anti HER2 terapiji (46.8% vs 27.6%, 20.0% z samo enim anti- zdravilom)

► EFS in OS nista različna med skupinami



de Azambuja E, et al. Lancet Oncol. 2014;15:1137-1146

NeoSphere: načrt in cilji raziskave



- **Primarni cilji:**
  - Primerjava deležev bpCR
  - TD vs PTD
  - TD vs PT
  - PTD vs PD
- **Sekundarni cilji:**
  - PFS
  - DFS
  - Varnost
- **Druge analize:**
  - PFS glede na status hormonskih receptorjev
  - Povezava med PFS i tpCR

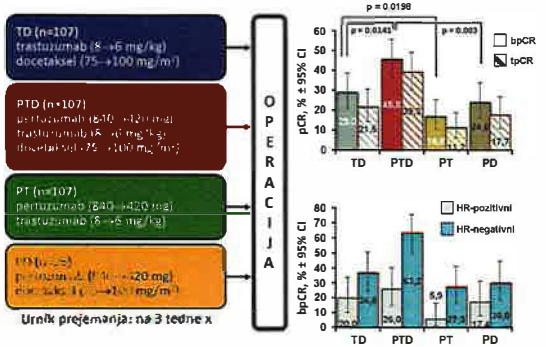
* operabilni = T2–3, N0–1, M0; lokalno napredovali= T2–3, N2–3, M0 or T4a–c, any N, M0; vnetni = T4d, in N, M0
RD, rak dojk; D, docetaksel; P, pertuzumab; T, trastuzumab
DFS, preživetje brez bolezni; pCR, patološka kompletna remisija; PFS, preživetje brez progresa;
pCR (tpCR) = ypT0/is, absence of invasive cancer in the breast, irrespective of ductal carcinoma in situ or nodal involvement;
skupni pCR (tpCR) = ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes, irrespective of ductal carcinoma in situ

Gianni L, *et al. Lancet Oncol* 2012; 13:25–32

NeoSphere: načrt in rezultati pCR

Bolniki z operabilnim ali lokalno napredovalim/vnetnim* HER2 pozitivnim rakom dojk

Kemo- naivni, primarni tumorji >2 cm (N=417)



HR, hormonski receptorji;
HR-pozitivni = estrogenski in/ali progesteronski receptorji pozitivni;
HR-negativni = estrogenski in progesteronski receptorji negativni

Gianni L, et al. Lancet Oncol 2012; 13:25–32

NeoSphere: dopolnilna sistemska terapija

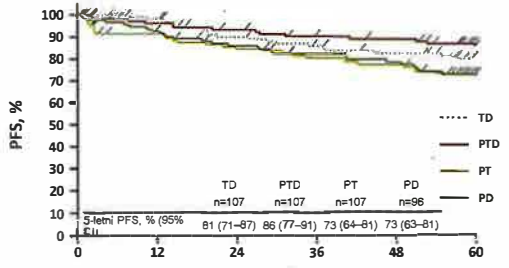
Bolniki z operabilnim ali lokalno napredovalim/vnetnim* HER2 pozitivnim rakom dojk

Kemo- naivni, primarni tumorji >2 cm (N=417)

FEC, 5-fluorouracil, epirubicin, and cyclophosphamide

Gianni L, et al. Lancet Oncol 2012; 13:25–32

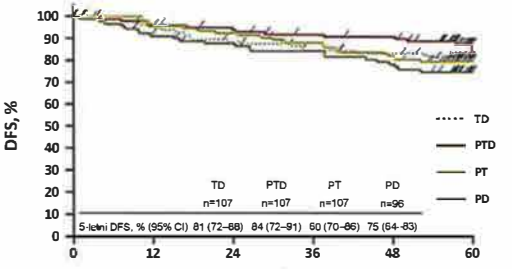
NeoSphere: rezultati PFS



n at risk						
TD	107	101	89	83	78	58
PTD	107	99	94	88	86	63
PT	107	93	86	80	77	55
PD	96	85	76	72	69	57

PFS=čas brez napredovanja bolezni (izhodišče opazovanja je randomizacija)

NeoSphere: rezultati DFS



n at risk						
TD	103	92	85	79	77	12
PTD	101	96	92	88	85	17
PT	96	91	87	81	75	10
PD	92	81	76	72	66	29

DFS=čas brez napredovanja bolezni (izhodišče opazovanja je operacija)

Trenutna priporočila predoperativne sistemske terapije za HER2 pozitivne rake

- Kemoterapija v sosledju antraciklinov in taksanov+ trastuzumab +/- pertuzumab (npr):
  - FEC na 3 tedne 3x→ $DOCE_{100}$ na 3 tedne 3x + trastuzumab +/- pertuzumab na 3 tedne
  - AC na 3 tedne x 4 → $DOCE_{100}$ na 3 tedne 4x + trastuzumab +/- pertuzumab na 3 tedne

KT zaključena do operacije!
Po operaciji nadaljevanje trastuzumaba do skupno 1 leta (+ HT pri HR pozitivnih

Zaključki

- Prednosti predoperativnega sistemskega zdravljenja danes so predvsem pretvorba neoperabilnih rakov dojk v operabilne in zvišanje deleža konzervirajočih operacij, ob enakem vplivu na dolgoročni izhod bolezni kot ga ima dopolnilno sistemsksko zdravljenje.
- Patološki popoln odgovor (ne glede na definicijo) napoveduje dober izhod bolezni, predvsem pri bolnikih s trojno negativnimi in HER2 pozitivnimi (HR negativnimi) raki.
- Čeprav patološki popoln odgovor ni dokončno razpoznan kot zadovoljiv nadomestni končni cilj v kliničnih raziskavah, pa je predoperativno zdravljenje privlačno za translacijske raziskave ter hitrejše in cenejše ovrednotenje učinkovitosti novih, predvsem tarčnih, zdravil.