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Dear Reader,

Welcome to a new and novel publication concept.

For most of us, publishing academic articles is time consuming and involves research that is often side lined by the clinical time required to treat patients properly. This does not detract from the huge amount of knowledge that doctors have around their various disease interests.

A platform for communication; a focus on “how we do it”; an opportunity to share ideas and understand what is happening in the community, pharmaceutical industry, and in our local and international meetings is needed in the “women’s health arena”. So when I was approached by Prof Christopher Szabo to take on the enormous task of setting up this publication based on the success of South African Psychiatry, I jumped at it (probably a little too naive about the job). There are 8 sections and each section editor is listed on the following pages with the ideas for the section.

Contributions are welcome from all and should you wish to be more involved then please send an email. Here is to the start of a journey; please join us for the ride

Carol Benn
Editor-in-Chief

Creating something is never easy but the end product is worth the effort. South African Women’s Health is no exception and it is very exciting to have been involved with the process leading to publication of this the first issue. The forerunner of this publication is South African Psychiatry www.southafricanpsychiatry.co.za which is about to enter its 4th year of publication, with myself as Editor-in-Chief. I look forward to many such years of involvement with South African Women’s Health as Associate Editor.

Christopher P. Szabo
Associate Editor
Professor Emeritus Franco Guidozzi is a Wits graduate and the erstwhile Academic Head of the Wits Department of Obstetrics and Gynaecology. He is a past President of the Society of Obstetricians and Gynaecologists, a Past President of the College of Obstetricians and Gynaecologists of the Colleges of Medicine of South Africa, a past president of the South African Menopause Society and a Past Secretary of the South African Royal College of Obstetricians and Gynaecologists.

He has published over 120 articles in peer reviewed and non-peer reviewed journals. He retired from the Wits Department of Obstetrics and Gynaecology in 2015, is still in fulltime private practice and enjoys reading, bonsai gardening and attending to his koi fish. He is married to Yolande, an advocate, has three daughters, all of whom are doctors, and loves laughing at himself.

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Prof Carol-Ann Benn is a Fellow of the College of Surgeons of South Africa with a special interest in Breast Disease. Her capacity as Head of the Breast Unit of Helen Joseph Hospital proves her long commitment to clinical excellence in this field of medical specialty.

Prof Benn offers service to society and the greater medical community, (both local and international), through her contributions, published and presented, and she is recognised internationally as a leader in Breast Disease. As lecturer in the Department of Surgery at the University of Witwatersrand, she contributes towards the education of healthcare professionals.

Through the organisation of foreign and private funding, Prof Benn was able to establish the Breast Health Foundation, various Breast Health Care forums and outreach programmes and is a representation on numerous Medical Boards and Health Care Committees. Prof Benn has paved the way for the improvement of women’s health care, has contributed towards the uplifting of women in society and has opened channels for public awareness of breast health.

She established the Netcare Breast Care Centre of Excellence at Milpark Hospital, Johannesburg, which co-ordinates national efforts for the specialised management of breast conditions to all women. In addition to her positions of responsibility, Prof Benn manages continuing research and research outputs. Numerous awards testify to her esteemed position in the medical field and in South African society.

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Dr Georgia Demetriou has been a Senior Consultant in the Division of Medical Oncology at the University of Witwatersrand Faculty of Health Sciences and Charlotte Maxeke Johannesburg Academic Hospital since 2004 and served as Acting Head of the Division from September 2013 to June 2014. She is Head of a General Medicine Undergraduate Academic teaching unit for the Department of Internal Medicine at Charlotte Maxeke Johannesburg Academic Hospital.

She has been local Principal Investigator and National Principal Investigator on 15 multinational clinical trials particularly in the field Breast Cancer. Dr Demetriou serves on the Executive Committee of the South African Society of Medical Oncology as Treasurer of the society, the South African Oncology Consortium Board of Directors as Chairperson of the board and on the Executive Committee of the Breast Interest Group of South Africa as the Chairperson of the committee.

She is an examiner, trainer and moderator for Certificate Medical Oncology for College of Medicine of South Africa sub specialist qualifying degree for Medical Oncology. Dr Demetriou has co-authored papers in peer-reviewed journals, as well as presenting at local and international scientific meetings. Women’s cancers and health in particular is a major focus of work.

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Dr Inge Kriel is an Oncology Care Physician affiliated with the internationally accredited Milpark Breast Care Centre of Excellence. She assists breast cancer survivors with screening for recurrence of the primary cancer and development of new cancers, management of late and long-term effects of cancer and cancer treatment, promotion of healthy lifestyle behaviours, and co-ordination of care with other oncology specialists, to ensure that patients receive the highest quality care.

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DR MARISSE VENTER

Dr Marisse Venter is a Plastic and Reconstructive Surgeon at Netcare Milpark Hospital. She has a special interest in breast reconstruction and cosmetic surgery. Her specialization encompassed 4 years of general surgery and a further 4 years of plastic surgery at the University of the Witwatersrand from where she qualified as a plastic surgeon.

She is registered with the Health Professions Council of South Africa as a Plastic and Reconstructive Surgeon, a member of the Association of Plastic and Reconstructive Surgeons of Southern Africa (APRSSA) and International Society of Aesthetic Plastic Surgery. Dr Venter has won numerous national and international awards for her research done on adipose tissue. Dr Venter has dedicated her life to the beautifying of women through breast reconstruction, facial, breast and body cosmetic surgery. All women deserve a body they would be comfortable with.

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PROF TESS VAN DER MERWE

Advisory Board member, Tess van der Merwe, is an Honorary Professor and Researcher in the Department of Endocrinology, University of Pretoria. CEO of the 11 Centres for Metabolic Medicine and Surgery of South Africa (CEMMS(SA)).

She is also the Director of the Waterfall City Hospital Metabolic Medicine and Surgery Centre Research group and is a full-time clinician at this hospital.

She was the Honorary Secretary of the International Association for the Study of Obesity for a period of 8 years and currently remains the Africa consultant for this association.

In addition, she is the Chair of the South African Society for Surgery, Obesity and Metabolism (SASSO) and has served this organisation for more than 25 years. Professor van der Merwe established the CEMMS (SA) in 2005.

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DR ANNA SPARACO

Anna Sparaco is a Wits graduate, having obtained a BSc Honours in anatomical sciences under the tutelage of Prof PV Tobias. After lecturing for 2 years in anatomical science, she entered her medical training at the Wits Medical School. After graduating, she spent 3 years in London at Guys and St Thomas’ culminating in gaining entrance into the Royal College of Surgeons of England. On returning to South Africa, she entered into a Hepatopancreatobiliary fellowship and concurrently was asked to join the Johannesburg transplant team and engaged in assisting in developing the liver transplant program.

To this end, and having been awarded the Miller Travelling Fellowship, she spent 3 months at the University Medical Centre in Omaha, Nebraska. Subsequently, she joined Prof Rene Adam at the Hospital Paul Bruix in France where she learnt about liver resection and finally visited Professor Buchler in Heidelberg where she was exposed to aggressive pancreatic surgery. She currently has a predominantly HPB practice at the Wits Donald Gordon Medical Centre and has recently co-founded the Centre for Digestive Diseases and Liver Health at the Rosebank Hospital.

With the establishment of South African Women’s Health, she was invited to subedit a section entitled “Women in Healthcare”. This coincided with the creation of the Women in Healthcare group who’s aim is to create a virtual and social networking platform for all women in medicine. Birth was given to this group because of the realisation that the current networking structure - both formal and informal - are predominantly directed towards the male gender as they have been the predominant participants in the work space and in fact still continue to be so. WIH will endeavour to host networking functions and also to host workshops that deal with social media and your practice, flow of money through your practice, medical aid fraud and so forth. The WIH section in the journal will aim at providing similar such information and also to look at the role and profile of women in medicine.

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NOTE: “instructions to authors” are available at www.southafricanwomenshealth.co.za
The launch of South African Women’s Health took place at Gabriella’s Tearoom on the 12th May 2017. Profs Benn and Szabo as Editor-in-Chief and Associate Editor addressed those present and provided background and motivation for the launch.

The event was well attended and included the following: Amy Reddy / Dr. Tarlia Govender (Roche), Adele da Silva / Olivia Curlewis (Cansa), Cathy Lepley (J&J / Meducat Medical), Christa Bester (Biotech Labs), Courtney Badenhorst / Jackie Martin (Nova Pharmaceuticals), Dario Bortolotti / Esmeralda Fouce / Shaldon Govender (Amgen), Gertrude Masebuku (MSD), Hilda McLaughlin (Takeda), Mandy Griesel (CR Bard), Maria Smith / Louise Greiling (GE Healthcare), Marlise Arndt (Novartis), Mzi Dubé / Preesha Premasagar (Sanofi), Taryn Purdon (Pierre Faber), Zane Vermaak (Nestle), Dr. Inge Kriel, Dr. Marisse Venter, Prof. Franco Guidozzi as well as Tibor Szabo (Nibbles and Bytes), Michelle Haskins (Thinkovate) and Vanessa Beyers (The Source).
We provide a specialised breast service to various hospitals and primary health care clinics within our Gauteng Province referral cluster but also see many patients who travel to us from other provinces across South Africa and other African countries. Although breast cancer is a very common malignancy among South African women, and sometimes men, access to specialised breast care is limited to very few centers. Many of our patients have experienced tremendous barriers when seeking help. These barriers include socioeconomic factors but also common barriers within our health care system.

We believe all women should have access to high-quality breast care irrespective of their geographic location and socioeconomic status and we are passionate about providing an excellent service to the community we serve.

In 2013, the breast clinic was taken over by Dr Sarah Nietz and the breast service was restructured and developed over the past few years. A second dedicated breast consultant, Dr Boitumelo Phakathi, joined and reinforced the unit in 2015. The number of patients seen in each Friday clinic have increased from about 30 to over 100 and the number of patients with newly diagnosed breast cancer have risen from under 50 per year to approximately 300 patients per year whom we diagnose, stage and treat within the unit. Long theatre waiting lists of over two months were reduced to about two weeks. We introduced surgical skills essential to contemporary breast care such as sentinel node biopsies and breast conserving surgery including advanced oncoplastic surgery. Although we have had to introduce a triage system to restrain the open access to our clinic, all urgent referrals are seen within the same week. Patients with clinically suspicious breast lumps have same-day imaging, biopsy and staging investigations to avoid delays in diagnosis. Our breast imaging unit was recently upgraded with new state-of-the-art imaging equipment and services include tomosynthesis, contrast mammography and breast MRI. Radiologists and surgeons meet on a weekly basis and review all imaging and biopsy results to carefully plan surgery and other treatment.

The management of breast cancer can be highly complex and is best treated by a team of specialists from the various disciplines involved. All patients with breast cancer are discussed in our weekly multidisciplinary meetings and the multimodality treatment is planned as a team approach. Our breast clinic teaches both under- and postgraduate students from the University of the Witwatersrand. We involve our students in our clinic with hands-on experience and teaching. In 2015, we introduced an electronic patient management program which allows us follow-up and audit and forms the basis of various research projects.

Our team meets weekly to review our research data and to discuss an academic breast topic of interest. Our main research focus is a NIH grant-funded multicenter project on HIV and breast cancer. The main outcomes will be to compare survival of HIV-positive versus HIV-negative women with breast cancer, to determine whether HIV + women are more likely to receive suboptimal cancer therapy than HIV- women and to evaluate determinants of suboptimal cancer therapy, as well as to determine whether HIV infection is associated with aggressive tumour biology and poorer survival by molecular subtyping. Other research interests include barriers to care and quality indicators of breast cancer care.

We face daily challenges but persist with a view that local challenges offer local opportunities and remain dedicated to provide a service of excellence and to promote onsite access, transition and coordination of multidisciplinary services.
INTRODUCTION

Axillary lymph node dissection (ALND) has historically represented a routine component of the management of breast cancer. The traditional benefits of ALND include the impact on disease control (i.e., axillary recurrence and survival), prognostic value, and an important role in planning treatment selection. The procedure is not however without morbidity and may result in lymphedema, nerve injury, and shoulder dysfunction, compromising arm function and quality of life.

The axilla is one of the most important prognostic factors in the treatment of breast cancer. ALND remains the standard treatment for women who have clinically palpable axillary nodes or positive nodes confirmed by ultrasound and guided fine needle aspiration or core biopsy.

Formal axillary dissection has slowly been replaced by sentinel lymph node biopsies (SLNB) in node negative axillas.

DEFINITIONS

The sentinel lymph node (SLN) is defined as the first regional lymph node that receives lymph flow from the primary tumour. It is the security guard (sentinel) and the first (again sentinel) that acts as the gatekeeper at the end of the driveway created by the body from the tumour. The sentinel lymph node (SLN) technique is based upon the observation that tumour cells migrate from a primary tumour to one or a few lymph nodes (LNs) before involving other LNs.

In patients with clinically node negative breast cancer, a negative SLNB identifies patients without further axillary node involvement, thereby reducing the need for more extensive axillary surgery.

HISTORY

The identification of the sentinel is based on the research of 2 specialists. Morton (1992) demonstrated the accuracy of the intra-operative mapping of the sentinel in patients with melanoma.

In 1993 a pilot series of sentinel lymph node (SLN) biopsies in breast cancer patients was published where the SLN was identified using a handheld gamma probe after injection of a radioisotope tracer around the breast tumour. This made it possible to identify the location of the sentinel node before skin incision and use the probe to guide surgery. This new technique complemented SLNB research using vital blue dyes that was being investigated in melanoma and breast cancer (Giuliano).

In the ensuing decades many studies have validated the accuracy and utility of SLNB; ensuring its place as standard of care in early node negative breast cancer.
IMPORTANT KEY TRIALS VALIDATING THE SLNB
(Please note number of patients accrued)

In a large phase III trial involving 5,611 women with breast cancer who had no clinical signs of axillary metastasis, researchers from the National Surgical Adjuvant Breast and Bowel Project, (a National Cancer Institute (NCI) clinical trials cooperative group), randomly assigned women to receive either a SLNB alone or SLNB plus ALND.

THOSE WOMEN IN THE TWO GROUPS WHOSE SENTINEL LYMPH NODE(S) WERE NEGATIVE FOR METASTATIC BREAST CANCER (A TOTAL OF 3,989 WOMEN) WERE THEN FOLLOWED FOR AN AVERAGE OF 8 YEARS.

Of relevance was the type of definitive breast cancer procedure as the majority of the women (87.5%) had breast-conserving surgery followed by radiation and the remainder had a mastectomy (no radiation required). Also of importance is that approximately 88% of the women also had adjuvant systemic therapy (either chemotherapy and/or hormonal therapy) and 82% of women in the trial received radiation therapy. The published results found no differences in disease free and overall survival, thus concluding that ALND was not required for women with clinically negative axillary lymph nodes and a negative SLNB mitigated the need for further axillary dissection.

A multicenter study of 443 patients with early breast cancer demonstrated that the SLNB technique could be learned and successfully applied by a large and diverse group of surgeons (both from private or academic practice). All patients underwent SLNB using radiolabeled colloid followed by completion ALND. At least one SLN was identified in 98% of cases and the predictive value of a negative SLN was 96%, with a false negative rate of 11% (sensitivity 88%). A more intensive pathologic evaluation of the nodes (false negative cases) utilizing deeper sectioning and immunohistochemical staining of the sentinel node increased the yield of occult metastases and led to an overall case conversion rate of 10.3%.

The ASCO expert guidelines panel performed a systematic review, including 69 eligible trials of SLNB in early stage breast cancer, a total of 8059 patients. SLN identification was successful in 95% of patients with a false negative rate of 7.3% (range 0 to 29%). Techniques used for SLN identification was either radiocolloid, blue dye, or both. The combination (radiocolloid and blue dye) resulted in a significantly higher success rate in SLN mapping with a lower false negative rate as compared to blue dye alone.

The NSABP B-32 trial, published after the above-mentioned systematic review, enrolled 5611 breast cancer patients with clinically negative nodes and compared SLNB followed by ALND vs SLNB followed by ALND only if the SLN was positive. Lymphatic mapping was successful in 97%, (false negative rate 9.8%). No significant differences were observed in regional control, overall survival, or disease free survival between the groups at a median follow-up of eight years.

The primary objective of the B-32 protocol was to determine whether axillary recurrence rates or systemic recurrence rates are higher in women treated with SLNB alone compared to ALND. The secondary aim was to determine whether patients with occult metastases on deeper sections, represent a population at increased risk for axillary or systemic recurrence.

Further axillary surgery when the sentinel is positive? Subsequently the American College of Surgeons Oncology Group, (another NCI clinical trials cooperative group), published an additional phase III clinical trial, testing whether women with a positive sentinel lymph node but no clinical evidence of axillary lymph node metastasis could be safely treated with no further lymph node surgery other than the SLNB. The Z-011 trial, which closed early due to poor accrual, only accrued 891 women who were randomly assigned to SLNB only or ALND after SLNB. Target accrual for the Z-011 study was 1900 patients. Low accrual and low event rate resulted in final patient numbers of 436 patients in the SLNB alone arm and 420 in the SLNB plus ALND arm. Note low accrual resulted in the study not being adequately powered to meet the predetermined statistical survival primary endpoint. All of the women were treated with breast conserving surgery followed by radiation therapy. Greater than 95% of the women received adjuvant systemic therapy (chemotherapy and or hormone therapy), and 90% received external-beam radiation therapy to the affected breast.

Recurrence rates in the ipsilateral axilla were similar between the two arms with four recurrences (0.9%) in the SLND alone arm compared with two recurrences (0.5%) in the SLNB plus ALND arm. Eleven patients assigned to the SLND only arm did have an ALND and 32 patients assigned to the SLNB plus ALND arm did not have an ALND. 20% of patients were lost to follow-up. 70% of patients had 11 (hormone receptor positive tumours (85%). Oestrogen receptor status
and adjuvant systemic therapy were independent predictors of survival. Postmedian follow-up of 6.3 years, the trial reported similar 5-year disease free and overall survival. (92.5% in the SLNB-only group versus 91.8% in the SLNB plus ALND group, overall survival) and (83.9% in the SLNB-only group and 82.2% in the SLNB plus ALND group, disease-free survival).

The conclusions reached suggested that SLNB alone is safe in patients who have a positive sentinel lymph node with no other clinical evidence of other lymph node involvement, as long as the breast cancer is treated with surgery, systemic therapy, and external-beam radiation therapy.

Based upon the apparent lack of regional benefit and low risk of events in this trial, completion ALND was deemed not necessary for all women with T1 tumours (clinically node negative), with less than three positive SLNs, who will be treated with whole breast radiation, particularly with oestrogen receptor positive tumours. When completion ALND is omitted in patients with a positive SLNB, whole breast radiotherapy is indicated. If partial breast radiation is planned, completion ALND should be performed.

THE REPORTED “EXCELLENT” OUTCOME IN THIS TRIAL FOR WOMEN TREATED WITH SLNB WITHOUT ALND IS AT LEAST IN PART DUE TO THE ABILITY OF LOCAL RADIATION THERAPY AND MODERN SYSTEMIC TREATMENTS TO EFFECTIVELY TREAT BREAST CANCER CELLS THAT MAY HAVE SPREAD TO OTHER AXILLARY LYMPH NODES BESIDES THE SENTINEL NODE. THE ARM MORBIDITY WAS LOWER THAN IN THE ALND ARM.

The AMAROS study involving 4806 patients (4766 were required) included all breast cancer patients with a T size from 0.5cm to 5cm, as long as clinically node negative. Patients went for primary surgery, and could have either BCT or mastectomy. The hypothesis was that radiation therapy provided local control and survival comparable to ALND with fewer side effects in women with a positive SLN.

The EORTC website is a great place to access the slides showing the randomisation and graphs of the outcomes. The recurrence rates, although underpowered, were extremely low in both arms showing the lack of need for axillary dissection in SLN positive patients undergoing radiation therapy. The secondary endpoints showed less morbidity in the radiation arm.

Clearly the greatest concern with SLNB is the potential of a false negative result, which could not only increase the potential for axillary recurrence, but also furthermore decrease the utilisation of adjuvant chemotherapy.

Interestingly, despite the documented 5 to 10% false negative rate seen in studies in which completion ALND has been done, several series report a low axillary recurrence rates after a negative SLNB (range 0 to 4.5%).

Despite variety in selection criteria and techniques for performing the procedure a SLN is consistently identified in approximately 96% of patients and furthermore predicts the status of the remaining axillary LNs in ≥95% of patients in most reported series. The false negative rate of SLNB was originally reported as 5 to 10% (with a sensitivity 90 to 95%), but consistently lower rates are seen when an experienced surgeon does the procedure.

National Cancer Database study of over 490,000 women with early breast cancer over a 7-year period from 1998 to 2005 showed the use of SLNB had increased from 27 to 66% in the United States. Similar results were reported from Canada and the United Kingdom. The American Society of Clinical Oncology (ASCO) and the International Expert Consensus Panel on the Primary Therapy of Early Breast Cancer have endorsed SLNB as an alternative procedure to ALND for the assessment of axillary metastases in patients with clinically node-negative early breast cancer.

UNDERSTANDING THE INFORMATION GAINED BY AXILLARY SURGERY

The SEER database of 213,292 female patients with breast cancer yielded the following rates of positivity of axillary lymph nodes for each breast tumour size:

- **T1a**: 7.8%;
- **T1b**: 13.3%;
- **T1c**: 28.5%;
- **T2**: 50.2%;
- **T3**: 70.1%.

The combined data from 13 published studies of SLNB (6444 successful SLNBs) demonstrated a false negative rate of 8.5 per cent. The LR of a negative test is 0.086.

According to the nomogram, the chances of missing a positive node for stage of cancer are as follows:

- **T1a**: 0.7%;
- **T1b**: 1.5%;
- **T1c**: 3.0%;
- **T2**: 7%;
- **T3**: 18%.

The risk of missing a positive axillary node can accurately be estimated for each stage of breast cancer using the LR, which is much more useful than the simple false negative rate.

Surgeons should use this information when deciding whether to perform SLNB and in their informed consent discussions(sentinels can be done irrespective of tumour size).
INVESTIGATIONS TO DO PRIOR TO THE PROCEDURE

Ultrasound plays a critical role in assessing the axilla (hugely relevant in our environment of HIV related lymphadenopathy). In women with clinically suspicious lymph nodes, preoperative axillary ultrasound (US) with fine needle aspiration (FNA) or core biopsy of suspicious areas provides a means to identify patients who have positive nodes, and thus may need (ALND) rather than a SLNB or be started on primary chemotherapy allowing for a SLNB post chemotherapy.

An experienced sonographer can count the number of positive lymph nodes. This information is critical in the MDM to determine the need for radiation therapy. In a series of 653 consecutive patients, the preoperative diagnosis rate of axillary disease was 23% using axillary ultrasound and FNA. This resulted in the avoidance of the need for two surgical procedures (first SLNB and second ALND in 150 women). The efficacy of this approach is somewhat variable between centers due to the accuracy of ultrasound being operator dependent.

DRAINAGE TO NON AXILLARY SITES

SLN techniques can identify non-axillary metastases (eg internal mammary nodes and intramammary nodes) in up to 43% of cases, depending upon the volume and type of colloid injected, injection technique and primary tumour location and size.

INTRAMAMMARY

Numerous case reports document the identification of intramammary lymph nodes on SLNB. Few studies however have explored the clinical significance of these lymph nodes. The incidence of Intramammary LNs ranges from 1 to 28% with most series reporting a high likelihood of additional axillary nodal metastases when the intramammary nodes contain cancer.

Therefore a staging ALND should be considered for women with a positive intramammary LN on SLNB, even if the axilla is clinically negative, because of the high rate of axillary LN involvement in these women.

INTERNAL MAMMARY

Positive IM nodes are most common with medial tumors over 2cm in size. Patients with axillary node negative disease will be found to have regional metastases to the IM nodes in 8 to 10% of cases. The diagnosis of positive IM nodes may affect treatment decisions regarding adjuvant systemic therapy and regional nodal irradiation.

The surgical management of the IM nodes remains controversial. There is no consensus as to whether there is a need for IM nodal biopsy in women with detection of an IM SLN. There are limitations to the SLN technique for identification of IM as interference from radioactivity at the primary tumour site may impede the ability of the surgeon to identify the drainage lymph node. There is a high rate of technical failure (20 to 39%). Surgeons who utilise only an intraoperative injection of blue dye to identify the sentinel nodes and who do not employ radiotracer injection will not identify IM drainage. Additional non-invasive methods for IM node assessment may provide assistance for the detection of these nodes. MRI and/or PET scanning may visualise IM nodes although confirmation of nodal involvement is clearly not possible.

The procedure should only be done if the management of the patient will be altered (such as):

1. Second primaries in patients who have previously had breast conservation and radiation therapy with drainage to an internal mammary lymph node may require adjuvant chemotherapy should the lymph node be positive.

2. If the procedure will alter the radiation field

3. Should the procedure not alter management, individual patient decisions should be made in conjunction with the multi-disciplinary team. IM biopsy can be accomplished with relative ease at the time of mastectomy by splitting the fibres of the pectoralis major. Patients undergoing breast conserving surgery usually require a second incision, which may leave an unsightly scar in the décolletage. The procedure itself may be complicated by pneumothorax, pleural effusion or bleeding.

Internal mammary nodes are not routinely dissected in patients undergoing breast conserving therapy or mastectomy with axillary lymph node dissection. Thus, in the absence of definitive data, dissection of the IM nodes with sentinel lymph node biopsy should be only done in specific indications as per patient discussion in the multi-disciplinary unit.

CHALLENGES IN PRIMARY CHEMOTHERAPY/ NEO-ADJUVANT CHEMOTHERAPY

The utilisation of primary chemotherapy as the gold standard in locally advanced breast cancers, and the expanding use of primary chemotherapy in a smaller resectable tumour (for example HER 2 neu positive tumour), results in the continual question as to when the procedure of SLNB should be done in patients who may be candidates for primary chemotherapy.

Most studies have restricted SLNB to T1 or T2 breast cancers <5 cm in size as it is expected that locally advanced and inflammatory breast cancer i.e. larger tumours will have a higher likelihood of positive axillary nodes.
Some studies have shown that SLNB is accurate in patients with T3 tumours and clinically and sonographically node negative axillae. It is for this reason many clinicians do not recognize large breast tumours as a contraindication to SLN dissection, as long as the axilla is clinically and ultrasound negative.

Much has been written on the use of sentinel lymph node biopsies post primary chemotherapy.

Patients with T4 tumours or inflammatory breast cancer are not considered candidates for SLNB, as the false negative rate is high, particularly in patients with inflammatory breast cancer. This is thought to be due to the partially obstructed, functionally abnormal subdermal lymphatics.

The 2005 ASCO guidelines on SLNB did not recommend the routine use of SLNB in patients with locally advanced or inflammatory breast cancer and rather an ALND was recommended to ensure loco-regional control.

Consensus recommendations from an International Expert Panel published in 2010 still considered inflammatory breast cancer to be one of the few absolute contraindications to SLNB. In addition, SLNB was not recommended for T4 tumours.

The optimal timing for (SLNB) in patients receiving primary therapy has been regularly debated; many because of the high reported false negative rate for SLNB performed post primary chemotherapy.

The 2011 NCCN guidelines recommended that SLNB be performed prior to primary chemotherapy because it provides valuable prognostic information for planning loco-regional treatment (particularly level of radiation or indications for radiation). Completion axillary dissection, if indicated, can be performed following chemotherapy at the time of definitive surgery. SLNB post primary chemotherapy can also be performed.

The ACOSOG trial Z1071, which is still accruing patients, is designed to answer the question of SLNB accuracy after primary chemotherapy.

2014 ASCO guidelines for sentinel lymph node biopsies and the NCCN guidelines for sentinels are available on both websites.

CHALLENGES IN DCIS

Issues in DCIS only revolve around concerns and risks as to micro-invasive disease and to reconstructive safety issues.

Most women with ductal carcinoma in situ (DCIS) do not require assessment of the axillary nodes if they are undergoing breast-conserving therapy. Women with DCIS may be candidates for SLN mapping if they are reconsidering undergoing mastectomy (due to size of DCIS, spontaneous nipple discharge, breast prostheses present or choice) because the performance of SLNB will be impossible at a later stage should invasive disease be found. An intact breast with its lymphatic plexus is necessary for injection of both the blue dye and the radioisotope tracers.

Further recommendations for SLNB in patients with DCIS irrespective of choice of definitive breast cancer procedure (breast conserving therapy or mastectomy) revolve around possible risk of node metastases. Nodal metastases risk is increased in patients with extensive high-grade DCIS, a strong suspicion of invasive disease based upon ancillary imaging, or documented micro-invasive disease in the core biopsy. Based on the data suggesting a SLNB can be performed post surgical biopsy, if a lumpectomy is performed and invasive disease is identified, a SLNB can be done as a separate operation.

CHALLENGES AROUND RECONSTRUCTION

In some cases it may be preferable to perform the sentinel node biopsy as a separate procedure before the mastectomy, especially if reconstruction is desired, so that the proper planning of type of reconstruction and need for radiation (post the 2013 consensus which stated there was a benefit for radiation in all node positive patients) can be determined prior to surgery so the patient is not faced with unknowns around risks of radiating prostheses (although many units now radiate expanders and prostheses, we prefer not to).

PREDICTIVE NOMOGRAMS FOR ESTIMATING RISK OF FURTHER INVOLVED LYMPH NODES

SLNB followed by a completion ALND results in significantly greater arm morbidity than SLNB alone. The majority of patients with SLNB metastases will not have additional positive nodes on completion of ALND, as a result several predictive nomograms for estimating the risk of additional positive nodes have been developed in an effort to spare women from unnecessary and potentially morbid surgery. These nomograms include both clinical and pathologic features, such as the size and/or number of the SLN metastases, extranodal extension, and the size and/or presence of lymphovascular invasion in the primary tumour.

A retrospective analysis of 319 patients with a positive SLNB who underwent completion axillary dissection compared the performance of four different nomograms. Unfortunately none of these nomograms was sufficiently reliable for clinical use.

SLNB IN SPECIAL CIRCUMSTANCES

Male breast cancer - The published studies of SLNB for breast cancer are in women. Data is limited...
in men with breast cancer (MBC), because male breast cancer is uncommon. A retrospective study of 30 men with breast cancer reported a 100% SLNB identification rate and a false negative rate of 0%. Prospective studies establishing the sensitivity and specificity of SLNB in MBC have not been carried out, due to paucity of numbers. However, the principles guiding SLNB seem to apply to men as well.

Due to the limited amount of data, the 2005 American Society of Clinical Oncology (ASCO) guidelines on SLNB did not make a specific recommendation about the use of SLNB in MBC, although it was deemed an “acceptable” alternative to axillary dissection in node negative patients.

**MULTICENTRIC DISEASE** - Studies evaluating the functional anatomy of lymphatic drainage support the theory that all quadrants of the breast drain into the same lymph node(s). Thus, subareolar and intradermal (rather than peritumoral) injection of radiolabeled colloid or blue dye render SLNB feasible for patients with multicentric disease.

Studies validating the success of SLNB in multicentric disease are small in number. In one study of 142 women with multicentric breast cancer, SLNB was successful in 91%, with a false negative rate of 4%. The number of patients requiring completion ALND because of a positive SLN is higher in multicentric breast cancer. The likelihood of finding additional disease at the time of completion ALND is also higher with multicentric disease. The ASCO guidelines recommend SLNB as appropriate for patients with multicentric disease.

**PREGNANCY** - the performance of SLNB during pregnancy has not been fully evaluated. Dyes such as isosulphan blue should be administered to pregnant women with caution due to the risk of anaphylaxis. Data assessing the dose of radiation to the foetus, suggests that there is minimal radiocolloid exposure during SLNB and 2011 NCCN guidelines conclude that radiocolloid is safe during pregnancy. Nonetheless, 2005 guidelines ASCO recommend against the use of SLNB in pregnant women with early stage breast cancer.

**MOST SPECIALISED BREAST UNITS DO HOWEVER PERFORM SENTINEL LYMPH NODE BIOPSIES IN PREGNANT WOMAN TODAY**

**PRIOR BREAST OR AXILLARY SURGERY** - The feasibility of successful SLNB in women who have undergone other non-oncologic types of breast surgery such as reduction mammoplasty or augmentation with breast implants or removal of accessory breast tissue is unclear. The expert panel convened by ASCO did not make a recommendation for or against SLNB in women who have had breast reduction or augmentation because of insufficient data. They suggested that if SLNB were considered in this setting that it might best be performed with preoperative lymphoscintigraphy. SLNB after axillary surgery has not been widely studied. In one retrospective series, a SLN could not be identified in 25% of 32 cases in which SLNB was attempted in women who had undergone prior axillary surgery. Guidelines from ASCO recommend against SLNB in women who have undergone prior axillary surgery.

With regard to patients having a local breast cancer recurrence, there are accumulating reports of successful second SLNB in these patients in whom a previous SLNB and/or axillary dissection has been performed. This technique is being more frequently employed and studies assessing the success of this procedure are indicated. Lymphoscintigraphy should be performed if repeat sentinel node biopsy is planned, so as to successfully document the alternate drainage patterns.

**CHALLENGES WITH MICRO-METASTATIC DISEASE**

In 2012, we were still debating although we have a better understanding now of the clinical significance of micrometastases in breast SLNs. Micrometastases include all metastases 2.0mm in greatest dimension. Isolated tumour cells (ITCs) are defined as cell clusters or single cells with no single cluster larger than 0.2mm. A recent analysis of population-based data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) national cancer database showed that the presence of micrometastases no larger than 2.0mm in lymph nodes is associated with an overall decrease in survival at 10 years of 1, 6, and 2% for T1 (no larger than 2.0?cm), T2 (larger than 2.0?cm but no larger than 5.0?cm), and T3 (larger than 5.0?cm) tumours, compared to patients with no nodal metastases detected. This SEER analysis included data prior to the advent of the widespread use of SLN biopsy.

The study showed that in women with a mammographically detected tumors <2.0cm, there is little outcome significance associated with the presence of micrometastases. The study does suggest that for larger tumours, detection of micrometastases may be more relevant in terms of clinical outcome. Considering this is a population-based study, concerns as to how the nodes were sampled (possibility of both micrometastases in larger tumours confirming aggressive intrinsic biology or rather suggesting undetected macrometastases deeper in paraffin blocks) must be considered.

A large retrospective analysis of pre-SLN era data from California and Massachusetts showed no impact on 15-year mortality estimates in any tumour size category when only a single lymph node contained a metastasis, regardless of primary tumour size. In that analysis, the median metastasis size was 6.0mm. This study supports the hypothesis that the primary
tumour biology has more prognostic importance than a minimal lymph node tumour burden.

When a SLNB is not successful or when clinically suspicious nodes are encountered in the axilla the surgeon should perform an axillary dissection for staging purposes and to ensure locoregional control.

TECHNICAL CHALLENGES

Injection of Colloid and Dye

Both success and accuracy of SLNB are increased with the combined use of blue dye and isotope.

Currently the new kid on the block is sienna-sentimag (see following article). SLNB success decreases with increasing body mass, tumour location, surgical biopsies, and non-visualisation of hot nodes on the pre-operative lymphoscintigraphy.

PATHOLOGICAL INTERPRETATION

Smaller volume of pathology tissue received during SLNs compared with an axillary dissection has prompted more comprehensive lymph node analysis increasing detection of micrometastasic disease. Data analysis shows that many women previously classified as having node negative axillas are now classified as having minimally node positive disease.

AS A RESULT, OUR NODAL CLASSIFICATION AND CANCER STAGING HAVE EVOLVED TO RECOGNIZE A STRATIFICATION OF NODAL TUMOUR BURDEN RATHER THAN A SIMPLISTIC POSITIVE AND NEGATIVE.

The more sections we evaluate from SLNs the more metastases we identify.

It may be impractical to expect the practising pathologist to mount, stain, and microscopically examine every section through the SLN paraffin blocks, unless the data received will impact on treatment protocols and outcome. Despite recommendations from the College of American Pathologists and the American Society of Clinical Oncology, there are still variations in the approach to SLN evaluation by pathologists. What is needed is adherence to a standardized evaluation protocol.

The most important aspect of the sentinel node examination is careful attention to slicing the SLN no thicker than 2.0mm with correct embedding of all the slices to assure we identify all macrometastases (>2.0mm). A single section from blocks prepared in this manner will identify all macrometastases present but smaller metastases may be missed. The prognostic significance of these missed micrometastases is under continual evaluation. Numerous studies analysing the discordance between frozen section imprint cytology at the time of the procedure demonstrate that best assessment of the sentinel lymph node pathology is determined in the laboratory by definitive histology. Most units do not do intra-operative assessment of the SLNB today.

Management of Sentinel Lymph Node metastases

Approximately 40% of patients with a positive sentinel lymph node (SLN) will be found to have residual disease in the axilla.

By definitions occult disease is not detected on routine H&E, but rather on IHC staining.

1. Isolated tumour cells (ITC) are not considered an indication for further axillary surgery, radiation treatment or adjuvant systemic therapy. It should be noted that finding ITC in lymphatics as a result of iatrogenic displacement from core biopsy procedures has been documented and is not considered to be clinically significant.

2. Micrometastases - patients with micrometastases are considered node positive and therefore it seems should result in a worse prognosis. Most studies, however show no change or only a small reduction in patient survival compared with those without micrometastases.

Pathologic evaluation of sentinel lymph nodes for occult metastases in a randomized trial of 3887 women who underwent SLNB alone or SLNB plus ALND for invasive breast cancer detected occult metastases in 16% of patients (ITC clusters in 11%, micrometastases in 4%, and macrometastases in 0.4%).

The following findings were noted:

- Occult metastases were an independent adverse prognostic factor with an increased risk of distant disease and death.
- The risk associated with ITC was less than that of micrometastatic disease.
- Five year analysis showed small but statistically significant outcomes for patients with and without occult metastases with respect to overall survival (95 versus 96%), disease free survival (86 versus 89%), and distant disease free interval (90 versus 92%).
- The presence of occult metastases was not a negative predictive factor; 85% of women with occult metastases were alive without breast cancer recurrence at 5 years.
Results from the American College of Surgeons Oncology Group (ACOSOG) study Z0010, a prospective multicenter study of 5210 patients with almost eight-year follow-up, confirm that IHC-detected metastases have no significant impact on overall survival.

Thus, routine IHC or PCR is not recommended for the evaluation of SLNs in guidelines published by ASCO, and NCCN. Histologically negative nodes that are IHC or RT-PCR-positive are classified as pN0 disease in the TNM staging system for breast cancer.

Guidelines from ASCO and NCCN recommending that routine completion ALND be carried out for micrometastases detected on SLNB with standard hematoxylin and eosin (H&E) examination, have recently been questioned particularly for women with less than three positive lymph nodes.

**CHALLENGES WITH POSITIVE SENTINEL NODES**

Macrometastases - The 2005 American Society of Clinical Oncology (ASCO) guidelines and 2010 National Comprehensive Cancer Network (NCCN) guidelines recommended that routine completion ALND be carried out for patients with SLNB macrometastases (≥2 mm).

The recent publication of the Z0011 trial has resulted in less indications for a completion ALND in patients with a positive sentinel lymph node whom are undergoing BCT and WBR. Role of IHC in invasive lobular carcinoma is an important concept. IHC staining with cytokeratin can be helpful for examination of the sentinel nodes in patients with invasive lobular carcinoma since the morphology of lobular cancer can be difficult to detect on H&E assessment of axillary lymph nodes.

**SENTINEL NODE BIOPSY POSITIVE, WHEN SHOULD COMPLETION AXILLARY DISSECTION BE PERFORMED?**

The need for completion axillary lymph node dissection (ALND) in women with clinically node negative T1 or T2 tumours is dependent upon the SLNB findings. There are some clear indications some controversial ones

**No nodal dissection is needed when:**

- In patients with a negative SLNB
- ITC on SLNB

**Performance of nodal dissection is accepted in:**

- Micro or macromet in 3 or more nodes detected with standard (H&E) examination (recommended for both staging and local control)

- The timing of the ‘procedure one’ procedure versus delayed (SLNB followed by second procedure, completion ALND) does not seem to impact the total lymph node yield or the rate of long-term complications (particularly lymphedema).

** Mostly no dissection needed**

The SLN is the sole tumour-bearing node in up to 60% of women who have a clinical and ultrasound node negative axilla and in almost 90% of patients who harbour only micrometastatic disease.

Completion ALND in patients with a positive SLNB showing micrometastases or macrometastases in less than three nodes probably is not needed. Speculation that completion ALND may not be necessary in selected patients with a positive SLNB in less than three nodes because the need for systemic therapy is established has already been considered in the Z011 trial and AMAROS. The risk of an axillary recurrence appears to be low particularly in patients receiving WBR.

The NCCN has not changed their guidelines and continues to recommend completion ALND for all women with positive sentinel nodes until additional randomized trial results are available. It is critical that the distinction can be made between isolated tumour cells, micrometastases, and macrometastases and is made in terms of clinical management, (at least a 22% misclassification of sentinel node metastases has been demonstrated).

Omission of the ALND can be considered if the tumor burden appears low (cases with isolated tumour cells or micrometastases) when whole breast radiation with high axillary tangents is planned. Results from two ongoing randomized trials studying the benefit of ALND for clinically node negative women with positive SLNs: the EORTC 10981-22023 AMAROS trial; and Trial 23-01 show ALND is probably not needed.

**WOMEN WHO ARE HAVING MASTECTOMY RATHER THAN BREAST CONSERVING THERAPY SHOULD BE COUNSELSLED THAT THEY MAY NOT NEED A COMPLETION ALND IF THE SLNB IS POSITIVE, BUT MAY NEED POSTMASTECTOMY RADIATION.**

**ANOTHER CRITICAL PROBLEM IS THAT WOMEN WHO UNDERWENT PRIMARY CHEMOTHERAPY WERE EXCLUDED FROM THE Z-011 TRIAL, AND THEREFORE RESULTS OF THIS TRIAL COULD NOT BE EXTRAPOLATED TO THESE PATIENTS.**
• T1, hormone receptor positive tumours, in women who are comfortable with some level of uncertainty about long-term outcomes, avoidance of completion ALND is an option.
• When completion ALND is omitted in patients with a positive SLNB, whole breast radiotherapy is indicated. If partial breast irradiation is planned, completion ALND should be performed.
• Women who are having mastectomy rather than breast conserving therapy should be counselled that a completion ALND is not necessary if the SLNB is positive as long as postmastectomy radiation is performed.
• In cases where prosthetic reconstruction is desired, it may be preferable to perform the sentinel node biopsy as a separate procedure before the mastectomy. If there are concerns regarding proper sequencing as to the type of reconstruction (autologous or prosthetic, or immediate or delayed) and radiation, these need to be arranged and discussed in the MDM.
• The use of sentinel node biopsy in patients with locally advanced disease, or patients undergoing primary chemotherapy with ultrasound node positive axilla, can be performed post primary chemotherapy

• Use of SLNB in pregnant patients, and those who have had prior breast or axillary surgery can be done but remains controversial.
• Inflammatory breast cancer is one of the few absolute contraindications to SLNB

Consensus on tumour biology and SLNB may take decades, due to the numerous biologic subtypes of breast cancer such as ‘triple negative’ basal phenotype tumours and Her2/neu overexpressing tumours. Minimal nodal tumour burden may have a different significance for these patients compared to Her2 negative, oestrogen receptor positive patients.

**BIGGEST CHALLENGE OF ALL**

Realizing that the SLNB is merely a tool, and breast cancer is a systemic disease, understanding the information gained by the sentinel lymph node biopsy may ensure an increase in time taken to guide women undergoing the trauma of a breast cancer diagnosis as to what oncological treatments they require and counsel them as to the risks of certain reconstructive procedures.

### References

NCCN guidelines 2011; 2016
NSABP trials
ACOSOG studies 2010:2011;
AMAROS SEER data analysis

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## Sentimag®

**Magnetic sentinel lymph node localisation**

A new standard of technology has been developed to assist in identifying sentinel lymph nodes; Sentimag and Sienna are currently widely available across Europe, Australasia, Singapore and Hong Kong and was launched in South Africa in February 2017 by Sysmex South Africa.

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Women in healthcare (WiH) is a networking group aimed at creating an informal platform to empower women to achieve their potential in the healthcare industry. It is clear in all professional spheres that the workplace which has been formulated to suit a demographic profile, may not have evolved to accommodate the relatively new admission of women in this sphere.

Despite the increasing numbers of women entering the previously male-dominated health professions, few academic centers have a critical mass full of women professors, much less women leaders. Recent figures quoted by the Transformation committee of the University of the Witwatersrand is 8%. (verbal communication).

It is well known that women tend to be more modest about their achievements and they are less apt than men to see themselves as qualified for top positions even when their credentials are equivalent or superior. Moreover, informal networks for women are less extensive and less likely to include colleagues or higher-ranking people from previous institutions.

Many women remain isolated due to the lack of this “social capital” and essential information that grows out of developmental relationships is often more difficult to access. Isolation further reduces the capacity for risk-taking, often translating in a reluctance to pursue professional goals and often results in a defensive and protective response. It is significant that some women experience isolation at work whereas for most male health professionals work tends to be more social. This paradox is compounded when similarly isolated women are appointed as tokens to committees and often there is a paucity of role models.

An interesting phenomenon was evident in the process of developing WiH. Enthusiasm and support for the concept is predominantly mid to late career women who identify with the need for such a networking platform. The feedback from many of the younger generation or newly qualified professionals has been that the gender inequality does not exist. The gender inequality seems to only become apparent when women professionals mature in their careers and realize that the playing field is not necessarily equal.

Dr Phakathi mentions in her article the need to network. Currently the networking platform is such that it addresses and suits the networking needs for the dominant professional demographic. These networking opportunities usually occur informally around sport on TV in the doctors’ room, football games, a golf course and drinks at the pub. Women may not necessarily feel comfortable or welcome in this environment. WiH is intended to provide an informal virtual and social platform to facilitate creating a professional network and supporting the development of mentors for emerging talent. Networking events will be organised and opportunities will be created for sharing information and facilitating interpersonal connections.
How can one advance her skills and excel in a male-dominated industry? The answer lies within us - IT BEGINS WITH US, it begins with us developing and advancing ourselves personally: SELF-ADVANCEMENT.

In order for things to change in your life, you need to develop into the person ready for that change. After developing personally, then you will have the confidence to face the world through advancing your career, one of the keys to unlock your greater and brighter future.

SELF-ADVANCEMENT/SELF-DEVELOPMENT

• Focus your time and energy on improving yourself. The key principle is to compete against yourself, being a better version of yourself than you were yesterday. Stop comparing yourself with others and stay focused in your lane.

• Know yourself. Know your strengths and weaknesses. Learn to depend on your innate capabilities and use them to your advantage. Learn on how to work around your weaknesses without letting them hold you back or deter you from attaining your goals.

• Believe in yourself, believe in the greatness that is within you. ‘The bird on the tree is not afraid of the branch breaking because its trust is not on the branch but on its own wings’—its innate strength and ability.

CAREER ADVANCEMENT

• The key is to never stop learning, learn as much as you can. You are the only one working on your career, therefore you need to take a full responsibility to succeed. Education is one of the strategies to promote women’s economic empowerment, thereby narrowing the widened gap between men and women in the workplace.

• Have a road map. Know where you are going, then you’ll be less likely to off-ramp along the way, you won’t be tossed back and forth in your journey to advance your skills. Decides on what you want for your career and focus your attention and energy in working towards reaching your goals.

• Get as much education and training as you can. Consider both formal (getting the highest degree you can possibly get) and informal ways (through career / leadership conferences, seminars, short term courses…). Learn a new skill or enhance the existing ones.

• If you aren’t learning, then you are definitely not adding any significant value in your workplace.
MENTORSHIP

AT THE WORKPLACE

• “One of your key successes is your ability to let others know who you are, what you have to offer and how you can make a difference” Caitlin Williams.

• Self-promote. Let your boss know about your future plans. Enquire from the boss which skills area you need to work on.

• Be proactive and go for what you want, even if it means asking for more responsibilities. Think about opportunities or improvements for the company. Work hard and prove yourself as an indispensable asset to the company.

• Identify the key competencies in your company, what your company/workplace stands for.

• Align your competencies with top management. Remember, as you look up to the top, those at the top are looking down, make sure they see you, not see you through the colour of your skin or your gender, but through the skill you possess and can offer.

• Build a good reputation for yourself, the reputation that befits that of senior managers.

• Recognise the value of your opinion and speak up in the meetings. When you believe in the value of what you want to share, others will also want to hear more. Avoid using an apologetic and uncertain tone when you speak.

• Have good relationships with your colleagues - you do need their support.

MENTORSHIP

• Successful people never reach the top alone. A mentor plays a significant role in your development thus make sure you choose them well. Look for a successful person, preferably in the senior position you are aiming for, someone who will be willing to nurture and help you reach your goal. This person may be within or outside your field of work.

• Break down the success of your mentor - what qualities do they possess that you may need to develop

• As much as you are being mentored, also look back and make yourself available to mentor those coming behind you

NETWORKING

• Networking is a crucial part in advancing in your industry. Network with those within and outside your industry. Surround yourself with the like-minded people.

In conclusion, as you rise up and advance your skills in the industry, lift up others as you rise for we rise further by lifting.

MICHELLE OBAMA ONCE SAID:

‘WHEN YOU’VE WORKED HARD, DONE WELL AND WALKED THROUGH THAT DOORWAY OF OPPORTUNITY, YOU DO NOT SLAM IT SHUT BEHIND YOU. YOU REACH BACK AND GIVE OTHER FOLKS THE SAME CHANCES THAT HELPED YOU SUCCEED’.

Dr Boitumelo Phakathi is a PhD candidate - University of Witwatersrand.
Correspondence: Please contact the relevant sub-editor as well as cc the Editor-in-Chief for more information.
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Human papilloma virus (HPV) causes 100% of cervical cancers.

HPV IS TRANSMITED BY SKIN ON SKIN CONTACT. UNLIKE HIV TRANSMISSION, A CONDOM IS NOT ENTIRELY PROTECTIVE FOR HPV. IT IS AN EXTREMELY COMMON VIRUS. ONE OF THE MOST IMPORTANT RECENT ADVANCES IN CERVICAL CANCER PREVENTION IS THE DEVELOPMENT OF A VACCINE.

Vaccination will have the most significant impact in South Africa where HPV prevalence is high and where there is low compliance to current screening programs. Even if patients are screened there is a high loss to follow up in the government sector and incredible anxiety created in private sector patients with high-grade lesions.

There are 2 approved vaccines available in South Africa. They should ideally be given prior to exposure. Both vaccines are approved for boys and girls from the age of 9. If administered before 14 years of age only 2 doses 6 months apart are required. If given after 14, 3 doses are needed. Gardasil covers HPV 6 and 11, which both cause genital warts and HPV 16 and 18 that cause over 70% of cervical cancers. Cervarix contains type 16 and 18. In April 2014 the South African National Department of Health implemented a school based HPV vaccination program for girls 9 years and older in grade 4 and above in public schools. School based vaccination programs in Australia and United Kingdom have achieved 70% coverage.

Both vaccines are not live attenuated vaccines but rather contain viral like particles. Their principal mode of action is to inhibit L1 receptors and inhibit entrance of the virus into the epithelial cell. In 2007 the quadrivalent vaccine was implemented to women from age 12 to 26 years in Australia. There was a progressive decrease in incidence of high-grade lesions in women over 18. In a large study conducted in Denmark involving 400,000 women born between 1989 to 1999; HPV vaccine was associated with a significant decline in genital warts.

THE PROTECTION FROM HPV VACCINE IS NOT CONFINED TO JUST CERVICAL CANCER BUT ALSO TO A DECLINE IN OROPHARYNGEAL CANCERS AND VULVAL AND ANAL CANCERS.

There is excellent safety data on both vaccines in large clinical trials with extensive post licensing data. The WHO global advisory committee on vaccine safety stated that the risk benefit profile is favourable and has warned against claims of harm that are raised on the basis of anecdotal reports in the absence of biological or epidemiological substantiation.

The only way to decrease cervical cancer is to vaccinate. Screening programmes do not work in low to low-income countries. Vaccination is the answer.
A BRIEF OVERVIEW OF THE GENITOURINARY SYNDROME OF MENOPAUSE

Franco Guidozzi

A BRIEF OVERVIEW OF THE GENITOURINARY SYNDROME OF MENOPAUSE

The lower urogenital tract including the vulva, vagina, urinary bladder and urethra, has an abundance of estrogen receptors which will, in an environment lacking estrogens as seen in the postmenopausal woman, result in atrophy of these organs producing significant symptoms and signs. These symptoms and signs not only occur in about 60-90% of postmenopausal women not on hormonal therapy, but may surprisingly also occur in 15-20% of postmenopausal women taking oral or systemic hormonal therapy as well as in 10% of premenopausal women taking the oral contraceptive pill.

Atrophy, particularly of the vagina, will occur in a number of other medical scenarios in the premenopausal woman, primarily seen in the postpartum period, in lactating women, women receiving GnRlh analogues, danazol and in about 50% of women with the Premature Ovarian Insufficiency Syndrome (new terminology for “the Premature Ovarian Failure Syndrome”).

PELVIC RADIOTHERAPY FOR VULVAL, VAGINAL, CERVICAL OR UTERINE CANCERS WILL RENDER WOMEN MENOPAUSAL, BUT IN ADDITION, IS PARTICULARLY UNKIND TO THE VAGINA AND INVARIABLY RESULTS IN SIGNIFICANT VAGINAL ATROPHY AND ACCOMPANYING SYMPTOMS & SIGNS.

The same applies to a large number of other cancer survivors who are rendered menopausal as a result of their therapy, becoming menopausal after completing their therapy, a scenario commonly seen in breast cancer survivors. Vaginal atrophy may also arise in cancer survivors simply because they become menopausal because of their age coupled with the impact of their treatment.

The erstwhile definition of “vulvo-vaginal atrophy” has been recently replaced by “the genitourinary syndrome of menopause” although the former continues to appear in most recent articles. The genitourinary syndrome of menopause is defined as a collection of symptoms and signs associated with a decrease in estrogen and other sex steroids resulting in changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra and bladder. The decline of estrogen in the vagina is closely correlated with decreased vaginal lactobacillus, increased pH, altered epithelial morphology, fragmentation of elastin, hyalinization of collagen fibres, reduced vascular flow and reduced fluid secretion in the vagina. The vagina will “shorten, narrow and its lining will become very thin”. Symptoms of the condition include genital dryness, soreness or burning, foul smelling vaginal odours, decreased lubrication with sexual activity, discomfort or pain with sexual activity, post coital bleeding, decreased arousal, orgasm,
TO DECREASE SYMPTOMS.

OR MASTURBATION HAVE BEEN SHOWN LINGONBERRY JUICE, INTERCOURSE AND /

SMOKING, DAILY USE OF CRANBERRY-

ESTROGEN THERAPY . CESSATION OF

MOISTURIZERS AND TOPICAL VAGINAL

MODIFICATIONS, USE OF LUBRICANTS OR

TREATMENT INCLUDES LIFESTYLE

rarely requires further investigations.

patient history and clinical examination only and

syndrome of menopause is invariably made on

Nevertheless, the diagnosis of the genitourinary

clothes and to rinse out the soap powder very well.

in sunlight soap only, separate from their other

deodorants in the vagina and wash their panties

only wear cotton panties, never use perfumes or

use only non- medicated and non-perfumed soap,

As a point of note, it is recommended that women

use only non- medicated and non-perfumed soap,

only wear cotton panties, never use perfumes or

deodorants, panty liners, spermicidals, lubricants or

tight / synthetic clothing may mimic or produce very

similar symptoms and must always be excluded in

cases not obviously clear cut.

Vaginal atrophy/genitourinary syndrome of the

menopause is commonly under-reported, under-

recognized, under-treated and is commonly referred to as “the silent epidemic”. There still are a

large number of women who consider it taboo to

openly discuss the condition and are therefore too

embarrassed to voice their symptoms. In dealing

with women complaining of the abovementioned

symptoms, it is always prudent to bear in mind that

inappropriate use of perfumes, powders, soaps,
deodorants, panty liners, spermicidals, lubricants or

tight / synthetic clothing may mimic or produce very

similar symptoms and must always be excluded in

TREATMENT INCLUDES LIFESTYLE

MODIFICATIONS, USE OF LUBRICANTS OR

MOISTURIZERS AND TOPICAL VAGINAL

ESTROGEN THERAPY. CESSATION OF

SMOKING, DAILY USE OF CRANBERRY-

LINGONBERRY JUICE, INTERCOURSE AND /

OR MASTURBATION HAVE BEEN SHOWN TO

DECREASE SYMPTOMS.

Vaginal lubricants such as Astraglide, K-Y jelly, Lubrin, H-R jelly, Surgilube or vaginal moisturizers such as “Replens” or “Moist Again” during intercourse all may alleviate symptoms. Phytoestrogens, vitamin E, oral pilocarpine and/or topical anaesthetics may have a role in some women, although they invariably are not very successful. Despite these recommendations, a significant number of women require further therapy and this primarily requires hormonal estrogen therapies. Systemic and oral hormonal therapy are very effective in reversing the symptoms and signs of the condition, although in about 15-20% of these women the characteristics will persist and the addition of topical hormonal therapy will be needed. Nevertheless there will be many women who will not accept systemic or oral hormonal therapy, and in these women topical vaginal estrogen therapy is the ideal option.

Older aged women not taking hormonal therapy are also an important cohort of women who will benefit greatly from topical vaginal estrogen therapy. Topical conjugated equine estrogen preparations, topical estrone creams or topical vaginal estradiol tablets are available in South Africa which are very effective in alleviating the symptoms and signs of the condition. There are two Cochrane Review articles published in 2006 and 2009 that have shown significant response and a very favourable adverse profile. Daily intravaginal application for the first two weeks and thereafter twice weekly of any of the above preparations will have a marked beneficial impact on symptoms.

WOMEN ARE TO CONTINUE THIS PATTERN WHETHER THEY ARE SEXUALLY ACTIVE OR NOT TO MAINTAIN THE BENEFITS. INVARIABLY, IT TAKES 3-4 WEEKS TO OBTAIN AN ACIDIC VAGINAL PH, 3 MONTHS TO IMPROVE VAGINAL LUBRICATION AND 2 YEARS TO SIGNIFICANTLY IMPROVE THE VULVAL BLOOD FLOW. WOMEN SHOULD BE COUNSELED THAT IT WILL TAKE ABOUT 4-6 WEEKS BEFORE ANY POSITIVE BENEFITS WILL BE APPARENT.

Topical vaginal products have also shown to decrease recurrent urinary tract infections. There may be minimal systemic absorption of estrogen in the first three weeks of treatment. Systemic absorption after 3 weeks of use does not occur and as a result, topical vaginal estrogen therapy will not alleviate vasomotor symptoms, have any impact on bones, cardiovascular system, breasts, etc. It is therefore plausible to use topical vaginal estrogen therapy long term in survivors of vulval, vaginal, cervical, breast, colonic, uterine and ovarian cancers who have symptoms associated with the genitourinary syndrome of menopause.

All studies published on this subject support the fact that topical vaginal estrogen therapy appears safe with no impact on disease free interval or overall survival of these cancer survivors. In fact, because the systemic absorption of estrogen is not an issue, long term use of topical vaginal estrogen is plausible and apparently safe in women irrespective of which cancer they have. Topical vaginal estrogen therapy also appears to be safe in breast cancer survivors taking tamoxifen. To put it more into perspective
with view to amount of estrogen used; by utilizing Vagifem 10 micrograms twice a week for one year is equivalent to only one and a half tablet of 1 mg Estrofem orally over one year.

Women who still have their uterus and use topical vaginal estrogen therapy do not require progestogen therapy to protect the endometrium. Topical vaginal estrogen therapy does not cause endometrial thickening. Specific advantages of vaginal application of estrogen therapy includes avoiding enterohepatic circulation, the lowest dose is very effective, does not lead to endometrial stimulation, does not require concomitant progestogen therapy if the uterus is still present, there are no clinically relevant systemic side effects and that it exerts primarily a local effect.

Recently, a few reports have been published in which the authors claim that Ospemifene (a serm) and Bazedoxifene (a serm in combination with conjugated equine estrogen) have improved vaginal symptoms and signs and more recently some research articles claiming that topical vaginal androgens and Erbium laser scarification of the vaginal lining may be alternative options in managing this condition.

IN CONCLUSION, EVEN THOUGH THE POSTMENOPAUSAL GENITOURINARY SYNDROME IS COMMON, TOPICAL-VAGINAL HORMONAL THERAPY IS VERY EFFECTIVE IN MINIMIZING OR ELIMINATING THE SYMPTOMS AND SIGNS IN 80-90% OF WOMEN WITH THE CONDITION. SYMPTOMS WILL RETURN ONCE TREATMENT IS STOPPED AND THERE DOES NOT APPEAR TO BE A LIMIT TO THE DURATION OF LONG-TERM THERAPY.

ELIMINATING THE SYMPTOMS AND SIGNS IN 80-90% OF WOMEN

REFERENCES

A SYNOPSIS OF THE SOUTH AFRICAN EXPERIENCE OF VAGINAL ATROPHY

Franco Guidozi

Knowledge pertaining to the prevalence and impact of vaginal atrophy on quality of life and on sexual function and relationships among South African women has not been known until very recently when the findings of the first study addressing these issues involving a total of 200 South African women and 200 South African men was published. The findings were published in an article entitled “Clarifying vaginal atrophy’s impact on sex and relationships (CLOSER) survey in South Africa.” in the journal CLIMATERIC in January 2017.

The participants were recruited from Johannesburg, Durban, Cape Town, Pretoria, Bloemfontein, Port Elizabeth and East London. They were interviewed utilizing a questionnaire which addressed the following

(a) symptoms of menopause and their impact on the women/relationships
(b) willingness to discuss vaginal discomfort
(c) the effects of vaginal discomfort on women, with emphasis on sexual relationships
(d) treatment of vaginal discomfort and its impact on sexual relationships
Women addressed their personal perceptions, symptoms and possible signs, whilst the men provided their knowledge of the condition and their views on how the condition was impacting on their partners and on their relationship and/or on their sexual activity and intimacy. About 64% of the participants were black, 16% were white, 14% were mixed race and 6% were Indian.

Hot flushes and night sweats affected 86% and 51% of women, whilst vaginal dryness affected 50% respectively. Other symptoms of vaginal discomfort reported included vaginal itching (38%), vaginal burning (24%), vaginal pain associated with touching and/or intercourse (21%), pain during urination (13%), vaginal soreness (12%) and bleeding during intercourse (6%). Menopause was said to be “worse than expected” in 29% of the women and among 21% of the men. Eighty percent of the women told their partners as soon as they were aware of the symptoms with 66% of the women and 77% of the men respectively feeling quite comfortable in discussing the subject. Seventy six percent of the women were likely to discuss their condition with their partners, 89% with their doctors and 58% with their pharmacist. Of note, black women were more likely to discuss their condition and its treatment with pharmacist.

Sixty percent of the women avoided intimacy because of the vaginal discomfort, while 62% of men claimed they had noted this avoidance of intimacy in their partners. Women volunteered that the most common reasons for this was because sex was less satisfying, more painful and their loss of libido. Twenty percent of the women and men interviewed believed that vaginal discomfort “had caused a big problem in their lives” particularly with view to sexual activity. A significantly higher percentage of women than men reported “being put off” sex and feeling emotionally distant from their partners and that vaginal discomfort and its other associated symptoms had a negative impact on their feelings and self-esteem. Over half these women felt they had lost their youth and were no longer sexually attractive. Sixty percent of the women were worried about the long-term effects of vaginal atrophy.

In this study, 40% of the women had used some form of treatment of which 26% were using lubricant gels or creams, 21% topical vaginal estrogen therapy, 20% mineral/vitamin supplements and about 10% systemic or oral hormonal therapy. The majority of women using the topical vaginal estrogen therapy stated that it had a positive impact on their sexual relationship, improving their sexual activity and intimacy. Seventy percent of these women felt more confident as sexual partners and “more woman”.

Encouragingly, the study shows that in South Africa, both women and men do acknowledge that vaginal atrophy has a significant negative impact on quality of life, particularly with view to sex and relationships, both emotionally and physically for most postmenopausal women and their partners. There was a significant decrease in sexual intercourse and an increase in avoidance of intimacy.

Women are prepared to discuss the impact of the condition on their physical and emotional wellbeing and are prepared to discuss the issue with their doctors, although a significant number of black women appear to first seek advice from their pharmacists. It therefore behoves all medical attendants to openly question their patients about the condition and address all possible sequelae and plausible treatment strategies.

Topical estrogen therapy significantly reverses the adverse symptoms of the condition. Starting treatment early and continuing long-term will have significant benefits. Adverse side effects topical estrogen therapy is most uncommon. Even though the study only included participants from metropolitan area, there is no reason to believe that management strategies would differ for women in rural areas.

In summary, the results and deductions derived from the CLOSER study are an attempt to address postmenopausal vaginal atrophy in Sub-Saharan women, a domain not previously researched. The reported effects of vaginal atrophy among South African women and men appear to be similar to women and men in Europe and North America, affecting adversely both physical and emotional relationships. Improvement however, is apparent after topical vaginal estrogen therapy.

From a South African perspective, while health-care access may be one of the major barriers to receipt of appropriate treatment for women affected by postmenopausal vaginal atrophy, raising awareness, including among medical attendants, is a priority to facilitate its appropriate management.

Reference
1. Guidozzi F, Thomas C, Smith T, Nappi RE. Clarifying vaginal atrophy’s impact on

Franco Guidozzi is an obstetrician and gynaecologist and an emeritus professor in the Faculty Of Health Sciences, University of the Witwatersrand. Correspondence: guidozzif@gmail.com
Over the next twenty years, cancer rates are set to increase six times faster in women than men.

Women are at an alarming increased risk of developing cancer within their lifetimes. To address it, civil society patient groups and Roche Products are collaborating to educate women and ensure that more women in Southern Africa are diagnosed at early stages.
Hope for women impacted by cancer

Women are disproportionately impacted by cancer throughout the world, both directly and indirectly, increasing the burden cancer places on society. At Roche we are committed to bringing new hope to women suffering from cancer through developing new innovative cancer treatments to women’s cancers.

Transforming treatment of HER2-positive breast cancer

Roche has been leading research into breast cancer for decades, and we remain committed to finding new ways to tackle the disease with the goal of improving patient outcomes and bringing them closer to cure. We were pioneers in introducing targeted therapies to HER2-positive breast cancer. These therapies have changed the natural course of the disease, to the extent that HER2-positive patients now experience better outcomes than those people with HER2-negative breast cancer.1 Despite this remarkable progress, there remains a significant need for additional treatments for people with this disease, as approximately half of people treated for HER2-positive advanced disease will experience progression of their cancer within 12.4 months of current standard treatment in South Africa,2 and a third of patients with early-stage breast cancer will eventually go on to develop advanced disease (metastatic).3 Targeted HER2 treatment options are therefore needed to allow these people to live longer and better lives.

Comprehensive take on cervical cancer

Human Papillomavirus (HPV) is the known cause of cervical cancer and is used to identify women at risk. Almost all cervical cancers – more than 99% – are caused by a persistent high-risk human HPV infection.4 Therefore, screening for HPV can help identify women at risk. Finding disease early, before cancer develops, is an important prevention strategy.5

The Roche Cervical Cancer Portfolio enables healthcare professionals to better screen, manage and diagnose women, based on the confidence and clarity of results across a continuum of patient care. The unique combination of molecular, cellular and tissue-based diagnostic tests provides healthcare professionals powerful information to make patient care decisions and minimise unnecessary treatment. Current treatment options include surgery, radiotherapy, chemotherapy, and more recently a biological therapy, or a combination of these.6

Biological treatment options to ovarian cancer

Being aware of the signs, symptoms and risk factors helps to diagnose ovarian cancer early and decide on the optimal treatment. Today, doctors may be able to diagnose ovarian cancer with greater certainty by combining advanced blood testing techniques, which help to better identify women at risk and pinpoint those women who need to undergo further investigation.7 Until very recently, treatment options were limited to surgery and chemotherapy. However, recent scientific breakthroughs mean newly diagnosed women or those with recurrent disease can now be treated with targeted therapies as well.8 As leader in cancer care, we continue on our journey to support women with this disease.

Tamika F. is a 12 year survivor of cervical cancer

3 O’Shaughnessy J. Extending Survival with Chemotherapy in Metastatic Breast Cancer; The Oncologist October 2005 vol. 10 Supplement 3 20-28
5 WHO. Human papillomavirus (HPV) and cervical cancer http://www.who.int/publications/ihl/nc/cervical-cancer/en/ Last accessed December 2018

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NEW FRONTIERS IN THE TREATMENT OF IRON DEFICIENCY DURING PREGNANCY & THE POSTPARTUM PERIOD

GLOBAL BURDEN OF ANAEMIA AND IRON DEFICIENCY

Anaemia is a common disease worldwide with more than 800 million people affected and more than half of this number have iron deficiency anaemia. The prevalence of anaemia is particularly high in both pregnant and non-pregnant women. On a global scale the burden of anaemia in both pregnant and non-pregnant women is greatest in the poorest countries with 56% of pregnant women having anaemia in the low to middle income countries (LMICs) versus 23% in high-income countries. Geographically the highest prevalence is in Sub-Saharan Africa and South East Asia. In South Africa after actions to improve anaemia the most recent prevalence of 42% lies between the developed and developing countries.

In the focus to reduce maternal deaths worldwide the relationship between the risk of maternal death and anaemia has been investigated. In the 2014 Saving Mothers report over 39% of all women who died due to pregnancy-related diseases were anemic, and 60% of deaths occurred in the postpartum period where haemorrhage was a major contributor (23%) to that figure. Bleeding after caesarean section is responsible for over 30% of maternal deaths due to haemorrhage.

More importantly more than half of all maternal deaths are considered to be avoidable. The major type of anaemia which is most common and avoidable is that of iron deficiency anaemia. In this context the importance of iron deficiency anaemia, particularly the diagnosis and treatment thereof, in pregnant women cannot be overemphasized.

IRON METABOLISM

Digestion of protein-containing food releases iron into the duodenum. From here it is absorbed into the enterocytes where some of the iron is stored while most is released into the bloodstream. Free iron is toxic with production of reactive oxygen species and free radicals which destroy lipids, membranes and mitochondria. Thus most of the iron is bound to transferrin – a transport protein produced by the liver. Transferrin has a number of sites for binding of iron and the amount of iron transported by transferrin overall can be determined by the transferrin saturation.

THE MAIN DESTINATION FOR THE IRON IS THE ERYTHROBLASTS IN THE BONE MARROW WHERE THE IRON IS INCORPORATED INTO HAEMOGLOBIN AND EVENTUALLY INTO NEW RED BLOOD CELLS.

Once the red blood cell is released into the circulation it generally lives for 120 days. Throughout that time it will pass through the spleen and tested physically as well as enduring hypoxia and pH changes. Only the strongest red cells survive – those that don’t will be taken up by macrophages that will, in a very efficient manner, use every part of the red cell. Proteins are recycled into amino acids and the iron taken up by the transferrin molecules is returned to the bone marrow.
Iron is stored in two sites: myoglobin in muscle (second largest store) and in the liver where excess iron is stored as ferritin (largest store). If the iron levels in the blood drop iron can be released from muscle and the liver thus maintaining the haemoglobin levels even when total body iron levels are low. Thus before the haemoglobin level drops the ferritin stores will be depleted. A loss of iron from the muscle, where it is needed for cellular repair amongst other functions, can lead to fatigue and weakness.

**BALANCE OF IRON METABOLISM IN WOMEN OF REPRODUCTIVE AGE**

With a normal intake of 20-30mg of iron per day only about 1-2mg will be absorbed. This intake is counterbalanced by a loss of 1mg per day lost as sloughing of enterocytes containing iron. Menstruating females lose about 2mg per day and absorb about 2mg per day assuming normal menstrual loss (Table 1). With menorrhagia the balance is lost and the potential for anaemia is increased.

**DURING PREGNANCY THERE ARE HAEMODYNAMIC CHANGES AND A PARTICULARLY HIGH REQUIREMENT FOR IRON. CIRCULATING BLOOD VOLUME INCREASES BY 50% AND ERYTHROCYTE CELLULAR MASS ONLY INCREASES BY 20% PRODUCING A DROP IN HAEMOGLOBIN – THE SO-CALLED HYDRAEMIA OF PREGNANCY. OVER THE COURSE OF THE PREGNANCY AND LACTATION THERE IS A SIGNIFICANT DRAIN ON THE IRON RESOURCES OF THE MOTHER.**

Even factoring in the lack of menstruation during this time there is a large deficit overall and the body can only absorb 2 mg per day. Thus a return to normal HB levels can be significantly delayed if there are low or absent stores before pregnancy.

**MEASURING IRON BALANCE**

The measures range from red cell indices to bone marrow aspiration – from the very cheap and less invasive to the very expensive and very invasive. Table 2 indicates the standard blood-related measures and the usefulness of each.

<table>
<thead>
<tr>
<th>HAEMOGLOBIN LEVELS</th>
<th>While all anaemias are defined in terms of a level of haemoglobin less than the reference range for age and gender, it should be noted that anaemia is a late sign of iron deficiency and already indicates depleted iron stores.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RED CELL INDICES</td>
<td>Microcytosis is a feature of iron deficiency anaemia but is not specific and can occur in a number of other types of anaemia such as 20% of patients with chronic infection or inflammation.</td>
</tr>
<tr>
<td>TRANSFERRIN</td>
<td>Measuring transferrin indicates how many potential transport proteins are available but does not reflect on how much iron is being transported. In iron deficiency more transferrin is produced by the liver creating a high transferrin level despite a significant iron deficiency.</td>
</tr>
<tr>
<td>TRANSFERRIN SATURATION</td>
<td>Measures the amount of iron carried by available transferrin molecules. A level less than 20% indicates a possible iron deficiency.</td>
</tr>
<tr>
<td>FERRITIN</td>
<td>If the ferritin level is below 30 mcg/l this indicates a very low store of iron which may occur even with a normal haemoglobin level. The best measure to diagnose early iron deficiency.</td>
</tr>
</tbody>
</table>

**IRON DEFICIENCY IN PREGNANCY AND WOMEN OF REPRODUCTIVE AGE**

The importance of good iron stores during pregnancy cannot be overemphasized. Apart from the subjective symptoms that the mother may have of fatigue and weakness, during pregnancy as well as in the post-partum period, a number of studies show significant effects on the foetus and the newborn. Thus there is an increased risk of intra-uterine growth retardation as well as preterm birth. If the child does not have sufficient iron at birth the physical and cognitive delay in these children continues even if the iron is replaced compared to those children who had sufficient iron at birth. A further point of concern is the increased risk of the mother requiring a blood transfusion, with concomitant adverse effects, if there is any haemorrhage during birth. There is also an increased risk of post-partum depression in women with anaemia during pregnancy.

The haemoglobin and red cell count must be measured at least once per trimester and before birth. However, because even at an adequate haemoglobin level the iron stores may be low, it is not
sufficient to measure haemoglobin. A ferritin level should also be taken at the start of pregnancy during the first trimester. If the levels are below 30mcg/l, iron stores are depleted and iron treatment is indicated even though haemoglobin might still be normal. A woman who starts a pregnancy with low iron stores must be treated with iron because the demand for iron will increase (Table 1).

A SPECIAL GROUP OF WOMEN ARE THOSE WHO HAVE HEAVY MENSTRUAL BLEEDING WITH A DESIRE FOR PREGNANCY. AS MENTIONED THEY ARE LIKELY TO BE IRON DEFICIENT ALREADY PLACING THEM AT SIGNIFICANT RISK DURING PREGNANCY AS WELL AS THE POST-PARTUM PERIOD. THESE WOMEN SHOULD BE ASSESSED AND TREATED FOR IRON DEFICIENCY IF POSSIBLE BEFORE ONSET OF PREGNANCY.

TREATMENT OF IRON DEFICIENCY

Maintenance of sufficient iron stores is important during two phases of pregnancy – the antenatal period when sufficient iron stores are required for growth of the foetus and the postpartum period when the strain on the mother, especially if breastfeeding, can be significant.

ANTENATAL THERAPY

There are two main iron replacement options: oral supplementation and intravenous iron. It is generally recommended that, unless other factors are present which make the rise in haemoglobin urgent, one should start with oral iron treatment in appropriate doses (a total of 160-200 mg/day given as two separate doses twice daily). If oral iron supplementation is given during pregnancy a recent meta-analysis of large randomised trials 7, showed that maternal anaemia was reduced by 70% although there was no difference in maternal mortality. Importantly, there was a significant reduction in the number of low birthweight newborns and preterm babies. Oral treatment of iron during pregnancy has even been shown to improve infant birth weight in an almost linear dose response fashion leading to a reduction in risk of low birth weight babies. For each 0.1 g/dl increase in haemoglobin an increase in birth weight of 14 g was observed.

The doses given are 200 mg per day on two different days for iron sucrose and ferric carboxymaltose. While safety profiles and responses in ferritin are similar between all three the following discussion covers iron sucrose and ferric carboxymaltose only.

In summary, the following clinical criteria indicate the need for intravenous iron treatment of iron deficiency in the second or third trimester of pregnancy:

1. Poor tolerance of oral iron – usually due to gastro-intestinal side effects

2. Lack of response to oral therapy (insufficient increase of haemoglobin or inadequate increase in transferrin saturation and serum ferritin levels)

3. Very low haemoglobin < 9 g/dl

4. Rapid increase in haemoglobin levels needed – e.g. very low Hb in third trimester, patients at risk of postpartum haemorrhage (PPH) or with religious reasons for refusing blood transfusions.

Intravenous (IV) iron can be given in three forms – low molecular weight iron dextran, iron sucrose and ferric carboxymaltose. While safety profiles and responses in ferritin are similar between all three the following discussion covers iron sucrose and ferric carboxymaltose only.

The doses given are 200 mg per day on two different days for iron sucrose and 1000 mg in a short infusion (over 15-30 minutes) as a once-off single dose infusion.
Some factors which may explain this increase in PPH rate are listed below:

a. Abnormal placentation – placenta praevia, low placed placenta, placenta accreta/increta/percreta

b. Caesarean section (depending on indication and number of previous C-sections)

c. Iron deficiency anaemia

d. Grand multiparity (> = 5 live births and/or stillbirths > 20 weeks gestation)

e. Advanced maternal age, obesity

f. Foetal macrosomia, polyhydramnios, multiple pregnancies

g. Pre-eclampsia, HELLP-syndrome

When comparing oral to IV iron therapy there is a clear difference independent of whether the oral iron is compared to iron sucrose or carboxymaltose. For both of the IV therapy formulations the ferritin level rises very quickly and remains high for a few weeks whereas there is very little if any increase in ferritin levels with oral iron preparations.9, 10

THE INCREASE IN THE HB AFTER IV THERAPY FOLLOWS A STEEPER ROUTE COMPARED TO THAT OF ORAL IRON THERAPY MAKING THE IV ROUTE BEST WHEN RAPID INCREASES IN IRON ARE REQUIRED. ALTHOUGH FERRIC CARBOXYMALTOSE DOES NOT CROSS THE PLACENTA, A SLIGHT IMPROVEMENT IN FOETAL HB AND SERUM FERRITIN MEASURED IN CORD BLOOD POST-PARTUM MAY INDICATE POSITIVE EFFECTS OF THE INCREASE IN IRON LEVELS IN THE MOTHER AND SUBSEQUENT TRANSFER OF IRON TO THE FOETUS.

POSTPARTUM IRON TREATMENT

An important indication for the use of intravenous iron to rapidly replenish iron stores is iron deficiency anaemia during the postpartum period. Reducing the risk of maternal mortality due to significant loss of blood after birth - as postpartum haemorrhage (PPH) – was identified as a national health priority in the South African Department of Health’s Saving Mothers campaign.3 Traditionally, significant loss of blood during birth was treated with blood transfusions but the capacity of the blood transfusion services and shortage of blood products nationally mean that an alternative needs to be available.

While the numbers of mothers dying due to postpartum haemorrhage is decreasing worldwide, the prevalence of post-partum haemorrhage appears to be increasing. Of additional concern is the finding that over half of maternal deaths due to postpartum haemorrhage were avoidable and were due to management lapses.11

In a group of over 800 000 women surveyed in Australia there was an almost 50% increase in PPH12 and in British Columbia there was an increase in PPH of 27% between 2000 and 2010.13

Patients who were treated with intravenous ferrous carboxymaltose in the post-partum period were more likely to obtain and sustain a haemoglobin level greater than 12 g/dl more rapidly than those taking oral iron. The response in haemoglobin was the same for iron sucrose and ferric carboxymaltose with similar levels of adverse effects.14

CURRENT RECOMMENDATIONS SUGGEST THAT HAEMOGLOBIN SHOULD BE MEASURED AROUND 48 HOURS POST-PARTUM AND IF THE LEVEL IS LESS THAN 9.5 G/DL INTRAVENOUS IRON TREATMENT SHOULD BE GIVEN. IN WOMEN WITH HAEMOGLOBIN LEVELS BETWEEN 9.5 AND 12.0 G/DL, ORAL IRON TREATMENT IS APPROPRIATE, PROVIDED THAT THE WOMAN TOLERATES THE TREATMENT WELL.
SUMMARY

IN CONCLUSION, MATERNAL IRON DEFICIENCY HAS SIGNIFICANT CONSEQUENCES FOR MOTHERS AND BABIES AND SHOULD BE TREATED. HAEMOGLOBIN LEVELS, RED BLOOD CELL INDICES AS WELL AS FERRITIN LEVELS SHOULD BE USED AS SCREENING TOOLS IN ALL PREGNANT WOMEN. FIRST LINE TREATMENT OF IRON DEFICIENCY IN PREGNANCY SHOULD BE ORAL IRON. THE DECISION ON WHETHER TO TREAT WITH INTRAVENOUS IRON NEEDS TO BE MADE BASED ON CLEARLY DEFINED CLINICAL CRITERIA WHICH INCLUDE TOLERANCE AND EFFECTIVENESS OF ORAL IRON, SEVERITY OF ANAEMIA, AND RAPIDITY WITH WHICH CORRECTION OF ANAEMIA IS REQUIRED.

Success of treatment should be assessed based on clear outcomes with improved haemoglobin and red blood cell indices, whereas ferritin levels are probably less helpful as treatment outcome measures. Pregnant women at risk for PPH should be prospectively identified during pregnancy and the haemoglobin should be increased with IV iron, if necessary, before birth.

Ferric carboxymaltose would appear to be the drug of choice to treat low iron stores in the second and third trimester of pregnancy and post-partum period given the available evidence from prospective randomised trials in pregnancy and postpartum.

Haematological indices should be checked 1-2 weeks after administration and if not sufficiently increased the infusion may need to be repeated. Administration of IV iron will improve haemoglobin and iron stores in a rapid, predictable and sustained fashion with a low rate of side effects when compared to administration of oral iron supplements.

The content of this text was presented at a scientific symposium at the Royal College of Obstetrics and Gynaecology congress in Cape Town in March 2017. The symposium was sponsored by VIFOR.

CONFLICT OF INTEREST:
All three authors received lecture honoraria and advisory board compensation from VIFOR Company.

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References:
Sample distribution was representative in terms of age, ethnicity, income etc. from populations in Johannesburg (46%), Pretoria (14%), Cape Town (15%), Bloemfontein (3%), Durban (13%), Port Elizabeth (8%) and East London (3%).

Results from the South African CLOSER survey revealed that vaginal discomfort is openly talked about amongst most South African couples. Notably, 89% and 58% of women were comfortable discussing vaginal discomfort with their doctors or pharmacies respectively.

A significantly higher proportion of black African women over white women (64% vs 42%; p <0.05) were likely to consult pharmacists about their symptoms. Furthermore, 87% of women would consult their healthcare provider if information about vaginal discomfort was sought.

The South African CLOSER study is the first South African study to report on the negative impact of vaginal atrophy on women’s sexuality and relationships.

Results from the original closer (Clarifying vaginal atrophy’s impact on Sex and Relationships) survey conducted in Europe and North America, highlighted the negative physical and emotional impact of vaginal atrophy on women’s self-esteem and relationships.

Due to a lack of information about the sexual welfare of postmenopausal women in South Africa, the South African CLOSER study was conducted.

200 postmenopausal women and 200 male partners of postmenopausal women were recruited.

IT IS THEREFORE CRUCIAL FOR HEALTHCARE PROFESSIONALS TO INITIATE DISCUSSION ABOUT VAGINAL ATROPHY TO ENABLE EARLY DETECTION AND APPROPRIATE MANAGEMENT OF THE CONDITION.
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Date of publication of promotional item: April 2016
Promotional material reference number: A0231.05/14v2
FOCUS ON

VAGINAL DISCOMFORT HAD A NEGATIVE IMPACT ON A RANGE OF RELATIONSHIP ISSUES

(a) Intimacy avoidance (sometimes or always)
- Women: 68%
- Men: 62%

We have sex less often
- Women: 52%
- Men: 51%

Sex is less satisfying for me personally (women)/Sex is less satisfying for my partner (men)
- Women: 33%
- Men: 26%

It puts me off having sex with my partner
- Women: 27%
- Men: 14%

I feel isolated from my partner as he doesn’t understand what is happening to my body (women)/I don’t understand what is happening to her body (men)
- Women: 24%
- Men: 17%

I feel emotionally distant from my partner
- Women: 21%
- Men: 17%

It has caused a big problem for our sex life
- Women: 20%
- Men: 18%

*p<0.05 (women vs men)

THE NEGATIVE IMPACT OF VAGINAL ATROPHY ON WOMEN’S SELF-ESTEEM WAS EVIDENT

(b) I feel I have lost my youth
- Women: 53%
- Men: 49%

I feel upset that my body noes not work as it did any more
- Women: 42%
- Men: 37%

It makes me feel old
- Women: 33%
- Men: 27%

I worry about the future of my sex life
- Women: 26%
- Men: 24%

I don’t feel sexually attractive any more
- Women: 23%
- Men: 23%

I have lost confidence in myself as a sexual partner
- Women: 20%
- Men: 20%

when I think about my sex life, I feel like less of a woman
- Women: 17%
- Men: 17%

When I think about my sex life now, I feel depressed
- Women: 21%
- Men: 21%

Vaginal discomfort has led to the end of sex as I know it
- Women: 20%
- Men: 20%

When I think about my sex life, I feel guilty
- Women: 18%
- Men: 18%

It makes me feel lonely
- Women: 17%
- Men: 17%

In 40 % of South African women, the symptoms of vaginal discomfort were left untreated.

VAGINAL HORMONAL TREATMENT HAD A SUBSTANTIAL POSITIVE IMPACT ON RELATIONSHIPS AND INTIMACY

Adapted from Guidozzi E et al, 2017

Adapted from Guidozzi E et al, 2017

Adapted from Guidozzi E et al, 2017

Adapted from Guidozzi E et al, 2017
VAGINAL ATROPHY

Vaginal hormone therapy improved sex lives, and couples became closer/less isolated from one another. In fact, 60 % of women receiving vaginal hormone therapy claimed to be optimistic about the future of their sex lives. 71% reported more confidence in themselves as sexual partners, 64% perceived themselves as “more of a woman” and 52% of women felt sexually attractive again. Many of these women were happy that their bodies were “working again” (76%), whereas 48 % of women felt rejuvenated. 1

Although many of the results regarding the effect of vaginal atrophy on relationships and self-esteem were similar to the results obtained from the CLOSER survey in Europe and North America, the proportion of women using local oestrogen therapy was substantially lower in South Africa (21 % in South Africa vs. 41 % in Europe and North America). 1

Sociocultural aspects and access to healthcare may be a consideration, and may be reflected by black African women being more likely than white women to consult pharmacists for information about vaginal atrophy, but less likely to have tried some form of treatment. 1

Promoting discussion about vaginal atrophy may enable healthcare providers to more effectively support affected women. 1

The International Menopause Society (IMS) Writing Group considers dialogue essential to enable early detection and appropriate management of the condition.

These recommendations also advocate starting treatment early, before the occurrence of irreversible atrophic changes. 1 Seeing that South African women and men are mostly comfortable discussing vaginal discomfort, and taking the substantial positive impact of vaginal hormonal therapy on relationships into account, healthcare professionals have not only an opportunity but also an obligation to initiate discussion around vaginal discomfort with their postmenopausal patients. 1

“ENCOURAGINGLY, THE RESULTS FROM SOUTH AFRICA SHOWED MOST OF THE INTERVIEWEES (WOMEN AND MEN) TO BE COMFORTABLE TALKING ABOUT VAGINAL DISCOMFORT.” 1

Reference:
In the last 8 - 10 years reconstructive surgeons have become more focused on minimizing surgical procedures and trying to maximize outcomes. There has been a large shift towards direct to implant reconstructions. The way these reconstructions are done varies according to geographical location and where the surgeons have been trained, but generally the breast mound reconstruction is performed with the definitive implant at the same time as the mastectomy. This does however require the careful pre-surgical oncological planning as the mastectomy needs to be a skin and potentially nipple sparing mastectomy.

PROSTHETIC BASED BREAST RECONSTRUCTION IN SOUTH AFRICA:
Currently this type of reconstruction is one of the most commonly performed post mastectomy reconstructions. They are often done as an expander prosthesis or 2 stage reconstruction, however there is a growing body of knowledge with one stage or direct to implant reconstruction and this reconstructive pathway will become the mainstay of prosthetic based reconstruction in the near future.

In SA we are fortunate to have access to implants and expanders for reconstruction in the state and training environment so younger surgeons are familiar with the use of these devices for reconstruction. In the private health care environment these devices are freely available and funded by most healthcare funders.
However there are certain devices that are not routinely funded. These devices are used to support the lower pole of the reconstruction and potentially to prevent implant malposition and displacement inferiorly below the infra-mammary fold. They are all biologically active materials and tissue-integrate in the course of the healing process. They are derived from dermis, either porcine or human, or are a type of synthetic mesh that tissue integrates. These meshes are made of various substances and there are multiple variations available. Most Direct to Implant (DTI) reconstructions performed in the first world will incorporate one of these devices for lower pole support of the breast reconstruction.

IN SA THERE IS LIMITED FUNDING FOR THESE MESH DEVICES SO WE HAVE HAD TO DEVELOP A RELIABLE DTI RECONSTRUCTION WITHOUT THEM². WE HAVE DEVELOPED THIS RECONSTRUCTION PROCEDURE THAT PROVIDES EXCELLENT ONCOLOGICAL MANAGEMENT, REMARKABLY GOOD COSMESIS AND GOOD LONG TERM DURABILITY.

This DTI reconstruction is always performed at the time of the mastectomy and is usually done via short lazy S incision from the areolar to the lateral aspect of the breast or a peri-areolar incision. These 2 incisions are used if the patient wants to maintain a similar sized post mastectomy volume. If the patient wants to be significantly smaller after her mastectomy and reconstruction, then the mastectomy is done as a type 4 SSM via a wise breast reduction pattern. The NAC can also potentially be saved even with this oncological incision. The implants used are generally shaped or anatomical implants as these shaped devices make a reconstruction that is more natural in shape than a round implant.

The upper 2/3rds of the implant is placed under the pec major muscle and the lower 1/3rd of the implant is covered by the inferior mastectomy flap. It is of utmost importance that the pec major muscle heals in this manner, otherwise there is a real chance of having a major reconstructive complication that can lead to implant loss. With the pec major muscle covering the upper 2/3rds of the implant there is usually very little rippling in this area of the breast reconstruction. There is however a certain amount of animation of the reconstruction when the patient moves her arms. This animation is often less than the animation seen in a sub-muscular cosmetic breast augmentation.

Fortunately this way of performing a DTI is very reliable and complications are unusual. The most feared complication is post-op haematomas and seromas. Implant rotation and displacement are fortunately very uncommon. However about 60% of patients will require a second day case surgery. This is usually to revise suboptimal scars and fat fill the breast reconstruction to repair contour defects and provide extra soft tissue cover to prevent rippling of the implant from visually distorting the breast reconstruction.

DIRECT TO IMPLANT BREAST RECONSTRUCTION IS BECOMING THE OPTIMAL WAY OF PERFORMING PROSTHETIC BASED RECONSTRUCTION AS IT IS RELIABLE, REPRODUCIBLE AND PROVIDES AN EXCELLENT BREAST MOUND RECONSTRUCTION IN ONE OPERATION.

SKIN AND NIPPLE SPARING MASTECTOMY:

The surgical treatment of breast cancer has evolved from radical mastectomy with routine removal of the nipple-areolar complex (NAC) to breast conservative therapy with preservation of the breast and NAC. When breast conserving surgery is not appropriate due to tumour related factors or the patient’s desire is for a mastectomy (either for risk reduction or cancer indications), conventional therapy still consists of mastectomy with removal of the NAC, followed by reconstruction. Rising interest in improved cosmesis has led to the introduction of the skin-sparing mastectomy techniques (SSM) and now nipple-sparing mastectomy (NSM) as alternatives to modified radical mastectomy.

The nipple areolar complex is regarded as the signature of the breast or likened to the tip of a nose and has significant aesthetic impact and has both sexual and psychological importance due mainly to its nerve sensation (erectile ability, erogenous sensation).

The current gold standard when required to do a mastectomy and reconstruction, is a skin sparing mastectomy and expander prosthesis reconstruction. This traditionally includes removal of the nipple areolar complex and the skin over the tumour (if required) so as to ensure clear surgical margins. There are three groups of patients for whom SSM is indicated. These are listed below

1. Patients who undergo the procedure for risk reduction (previously known as prophylactic mastectomies)
2. Patients with duct carcinoma in situ (DCIS)
3. Patient with invasive breast cancer
FOCUS ON

Clearly in patients undergoing risk reducing surgery with diverse indications such as confirmed BRCA 1 and 2, strong family history of breast cancer, atypical ductal hyperplasia, lobular carcinoma in situ and other risk lesions have extremely low recurrence rates irrespective of whichever technique is used. The reason for this is that the actual incidence of these patients developing breast cancer post mastectomy cannot be accurately quantified.

Looking at retrospective studies on patients undergoing SSM for invasive cancer or DCIS, the nipple is affected by tumour cells in only 5% - 10% of cases. It is for this reason that the concept of nipple sparing mastectomies has been proposed.

THERE HAS BEEN MUCH CONTROVERSY REGARDING THE ONCOLOGIC SAFETY OF NSM AS WELL AS THE INTRODUCTION OF A SET OF COMPLICATIONS, SUCH AS NIPPLE AND AREOLAR NECROSIS, THAT WERE NOT A CONCERN PREVIOUSLY WITH TOTAL MASTECTOMY. COMPPLICATING THESE ISSUES IS THE DATA ANALYSIS, THE LACK OF RANDOMISED CONTROL TRIALS, NO LONG TERM FOLLOW-UP, AND SMALL ISOLATED CENTRE BASED RETROSPECTIVE AUDITS.

Tumour contra-indication for nipple sparing mastectomies that are currently being considered includes the following list.

Patients with these disease processes should probably have a conventional mastectomy and not a nipple sparing mastectomy.

1. Paget’s Disease
2. Spontaneous nipple discharges with associated DCIS
3. Tumours close to the NAC
4. Multicentric breast cancers
5. Lobular breast cancers
6. Lymph vascular invasion
7. Inflammatory breast cancers
8. Over-expression of HER-2

Indications for nipple sparing vary from one institution to the next. The following indications have been taken from different institutions and are listed from safest to least safe.

1. High risk patients for bilateral SSM, as a risk reduction procedure
2. Small isolated DCIS away from the NAC
3. Small invading breast cancers, with some institutes giving tumour size up to 3cm
4. Axillary ultrasound and sentinel lymph node negative
5. 2cm distance from the nipple areolar complex

Looking at nipple sparing mastectomies in the risk reduction setting is critical as prophylactic mastectomy has been the subject of major publications by many international groups. Its oncology benefit is undisputed in patients with a genetic mutation.

NEVERTHELESS TO RECAP THE PRINCIPLES OF THIS SURGERY, ITS IMPACT ON QUALITY OF LIFE, ITS PSYCHOLOGICAL, AESTHETIC, SEXUAL, FUNCTIONAL AND PAIN REPERCUSSIONS ARE SUCH THAT IT SHOULD NOT AND MUST NEVER BE OFFERED IN AN EMERGENCY SITUATION.

Multi-disciplinary unit patient counselling involving discussions with other patients, onco-psychological assessment and discussions around the reconstruction should occur prior to patients undergoing the procedure. Immediate bilateral breast reconstruction by provisional or definitive implant with conservation of the skin flap and the nipple-areolar complex may constitute a positive radical issue for requesting and motivating patients at high genetic risk, managed by a multidisciplinary team.

Studies looking at patient satisfaction with objective observer assessments are few and far between. Important aspects to assess are appearance, symmetry, colour, position, and breast texture as well as nipple sensation and arousal.

Most studies are small, however most patients are satisfied with the appearance, symmetry, colour, position of the nipple and the breast texture.

RECONSTRUCTION
There is lower satisfaction amongst all patients with nipple sensation, with most patients rating this as decreased compared to their pre-operative sensation.

In conclusion, despite continued controversy and the need for more long-term outcome data, nipple-sparing mastectomy is a procedure that is gaining increasing visibility and acceptance. Provided that certain oncologic and practical criteria are instituted by the treating medical specialists, it has the potential for allowing less invasive surgery and improved cosmetic outcomes without increased oncologic risk in appropriately selected patients.

**NIPPLE SENSATION POST MASTECTOMY:**

A reconstructive surgeon is always going to strive to provide a patient with the optimal reconstruction. The reconstruction should look, feel and be as close as possible to the native tissue it is replacing.

The nipple areolar complex [NAC] is one of the most difficult appendages of the body to reconstruct. If the NAC is removed during a conventional mastectomy then it may be reconstructed at a second surgery.

This is usually performed via one of the below methods.

1] Chest wall skin and subcutaneous tissue for the nipple and a full thickness skin graft for the areolar.

2] Free nipple graft from the other nipple and tattooing for the areolar.

3] Other grafts: Ear lobe or Labia minora.

The modern skin sparing mastectomy may be performed safely with excellent oncological outcomes, and the areolar and often the nipple can be spared during this operation. It has significant reconstructive significance as the remaining areolar can be used to make a nipple or if the whole NAC complex is spared, then there is no need to reconstruct the NAC.

We are in the process of publishing a study on NAC sensation in the 3 mentioned settings.

1] NAC reconstruction post conventional mastectomy with expander prosthesis reconstruction where the NAC was reconstructed with regional flaps and a FTSG

2] NAC reconstruction using retained areolar for the nipple and a FTSG for the areolar.

3] NAC sparing mastectomy where there was no need to reconstruct the NAC.

The early results show that the first group has the poorest sensation which is similar to the rest of the breast mound. The other 2 groups show identical sensation of the nipple, much improved on the first group, but slightly less than normal skin sensation. It also stands to reason that the areolar of the group where it was saved in the NAC sparing mastectomy group had better sensation than the group where the areola was reconstructed with a FTSG.

As we further strive for the perfect breast reconstruction we must always make sure that oncological rules are strictly adhered to. The primary focus of breast cancer management is to strive to cure the patient. The reconstructive sequence comes as secondary to the cancer management. However, if the oncological rules are adhered to and the patient is treated in a multi-disciplinary breast health unit, the oncology and reconstruction can safely be performed to neither marginalize cancer management nor the reconstructive management of the patient.

**THIS WILL HELP TO ENSURE THE PATIENT IS MANAGED TO THE BEST OF OUR ABILITY AND TO ENSURE THAT THE PATIENT IS DISEASE FREE FOR MANY YEARS TO COME AND IS ALSO HAPPY WITH THE LOOK AND FEEL OF HER RECONSTRUCTION.**

References:

1. Complete One-Stage, Immediate Breast Reconstruction with Prosthetic Material in Patients with Large or Ptotic Breasts
   Donald A. Hudson, F.R.C.S., and Paul J. Skoll, F.R.C.S. Cape Town, South Africa. PLASTIC AND RECONSTRUCTIVE SURGERY, August 2002

2. Direct-to-Implant Breast Reconstruction without the Use of an Acellular Dermal Matrix Is Cost Effective and Oncologically Safe.

L C J Serrurier is a plastic surgeon. Correspondence: Please contact the relevant sub-editor as well as cc the Editor-in-Chief for more information.
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Breast implants are medical devices that are implanted under the breast tissue, chest wall muscle or breast skin and muscle. They are used to increase the size of breasts (breast augmentation) or to rebuild breast tissue after mastectomy or other defects during breast reconstruction. Silicone breast implants may also be used in revision surgery to correct or improve the result of previous surgery.

There are two types of breast implants approved for use, saline filled and silicone gel filled breast implants. Both types have a silicone outer shell. Today we mostly used silicone implants as we feel it provides an improved cosmetic appearance, durability and no possibility of spontaneous deflation.

Today the safety of silicone breast implants are well accepted albeit a long controversial history. In January 1992 the United States Food and Drug Administration announced a voluntary moratorium on silicone gel-filled breast implants and banned the use of silicone implants in the United States for a period of 14 years. The concern was regarding the...
possible cause of connective tissue disease, chronic inflammatory disease and cancer. Multiple clinical trials and investigations lead to the suspension of the moratorium and the FDA announcing the safety of silicone breast implants.

During this time South African surgeons continued to use silicone implants. Review of South African statistics of implants used during this time did not reflect an increase in disease processes associated with silicone implants.

In 2011, the FDA identified a possible association between breast implants and the development of anaplastic large cell lymphoma (ALCL), a rare type of non-Hodgkin’s lymphoma. Since 2011, we have strengthened our understanding of this condition and concur with the World Health Organization designation of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) as a rare T-cell lymphoma that can develop following breast implants.

The exact number of cases remains difficult to determine due to significant limitations in world-wide reporting and lack of global implant sales data. At this time, most data suggest that BIA-ALCL occurs more frequently following implantation of breast implants with textured surfaces rather than those with smooth surfaces.

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) develops in the fluid around the breast implant and is usually contained by the fibrous capsule around the implant; it does not develop in the breast tissue. The current risk is estimated to be 1 in 30 000 vs a risk of 1 in 8 of developing breast cancer. However documented cases of BIA-ALCL in smooth implants remains limited and some literature suggest it only occurs in textured implants. Because it is a rare disease it is difficult to be certain about the absolute risk of the disease.

THE MOST COMMON SYMPTOM IS A PERSISTENT SWELLING OF THE BREAST WITH OR WITHOUT AN ASSOCIATED BREAST LUMP. THESE SYMPTOMS DEVELOP BETWEEN 3 AND 14 YEARS POST INSERTION OF THE IMPLANT, MOST COMMONLY 8 YEARS POST-SURGERY.

The fluid is evaluated via ultrasound investigation and then sent for special tests. The majority of cases are cured with removal of the implant and associated capsule without the need of additional treatment. To date, there have been less than 400 cases worldwide with all of them having a 100% survival and cure rate.

All patients should be familiar with the potential complications associated with silicone prosthesis in order to make an informed decision.

SILICONE

Silicone is a naturally occurring element that has been manufactured so as to produce implants of various sizes and shapes. Silicone implants approved by the FDA are made of medical grade silicone. These implants undergo extensive testing to establish assurance of safety and effectiveness. The National Academies of Science, Engineering and Medicine concluded that “There is no evidence that silicone implants are responsible for any major diseases in the body.” See www.nap.edu. There is no known association between silicone implants and breast cancer.

WHAT YOU SHOULD KNOW ABOUT BREAST IMPLANTS.....

BREAST IMPLANTS ARE NOT LIFETIME DEVICES

The longer a patient has implants the greater the chances of developing complications, some of which will require more surgery. The “life” of these devices varies according to the individual. Some may need replacement surgery in just a few years, others may last 10-20 years and some even a lifetime. There are several different reasons why patients may need implant replacement surgery. Sometimes it is a matter of choice like size or implant style changes and sometimes removal and replacement is necessary because of a complication such as deflation, capsular contracture (hardening), pain or shifting of the implant.

MONITORING IS CRUCIAL .... MAMMOGRAPHY AND BREAST IMPLANTS

Breast implants make standard mammography difficult due to the displacement and atrophy of the native breast tissue. Thus it is important to inform your radiologist that you have implants. Special displacement views and additional views will be taken to improve the accuracy of the mammogram. Even in cases of bilateral skin sparing mastectomies, mammography is still necessary to evaluate and follow up any breast changes as well as implant characteristics over time.

A yearly ultrasound by a good radiologist will provide information regarding the integrity of the implant. I would recommend this investigation to be the determining factor as to when the implant should be replaced.

HOW LONG SHOULD I WAIT BEFORE I RESUME EXERCISE AND OTHER STRENUOUS ACTIVITIES?

During the first two weeks post surgery you should avoid soaking the wounds by avoiding bathing or showering. Overall avoid any strenuous exercise during the first four weeks and certainly while you
experience any pain or discomfort. The larger the implant you receive the heavier the breasts will be. You should wear good support bras while running to minimize pull on the skin and ptosis (drooping) of the breasts. I always recommend the use of two sports bras so as to minimize stretching of the breast skin.

TANNING SALON OR SUNBATHING

Tanning salons and sun bathing will not harm the implant but may worsen the scarring. You should avoid getting sun or tanning rays on the incisions for at least one year after the surgery as the UV rays may darken the incisions permanently.

THE EFFECT OF SMOKING ON THE HEALING PROCESS

Smoking causes the blood vessels to constrict, reducing the blood supply and the oxygen carried by the blood to the surgical area. The tissues need blood and oxygen carried by blood to heal. When the blood supply is reduced the tissues heal more slowly and are prone to bacterial infection. This may ultimately lead to skin necrosis or death of patches of the skin and poor scarring compromising the aesthetic result.

NIPPLE SENSATION, BREAST FEEDING AND UPPER BODY STRENGTH.

There will be changes in nipple and breast sensation after surgery. The feeling may increase or decrease and be different in different areas. The sensory changes may be temporary or permanent.

Thus there may be a loss of feeling around the inner aspect of the breast. If the implant was placed partially under the muscle there will be a permanent weakness in upper body strength which will affect patients performance.

Breast feeding will not be affected unless the breasts were lifted at the same time.

COMPLICATIONS

Below follows a list of some of the more frequent complications associated with breast implants

Local complications i.e. around the breast

- Haematoma formation, collection of blood
- Seroma formation, collection of body fluid
- Delayed wound healing
- Wound sepsis
- Peri-implant infection
- Sensory changes in the breast

Systemic complications.... your body

- Fluid and electrolyte abnormalities
- Deep vein thrombosis, clotting in the legs
- Postoperative lung complications

LONG TERM AND COSMETIC COMPLICATIONS... THE WAY IT LOOKS

- Rippling and contour deformities
- Malposition and displacement of the implant
- Asymmetries of the breast
- Capsular contracture (hardening of the implant, often painful caused by fibrous tissue around the implant)
- Visibility of the implant around its edges
- Implant rupture, which can cause the silicone gel to leak out into the neighbouring tissue or even parts of the body
- Pain, from many causes including muscles spasms and nerve injury
- Pain from a foreign body in your body

MY RECOMMENDATIONS ARE AS FOLLOWS: “IF WE WERE SUPPOSED TO HAVE SILICONE IN OUR BODIES WE WOULD HAVE BEEN BORN WITH IT. THUS YOU CANNOT EXPECT A FOREIGN BODY TO BEHAVE UNNOTICED IN YOUR BODY.” IT WILL FEEL UNNATURAL BUT SOFT MOSTLY, IT MAY BECOME HARD, IT WILL REQUIRE REPLACEMENT AND YOUR BODY MAY NOT ACCEPT IT ALL.

Please visit your surgeon once a year for a clinical examination and perhaps also have a breast ultrasound once a year. Please be sure to keep the original identification of your implant as you may need it for insurance purposes later.

Thus your initial decision making as to why you choose to have silicone implants should be solid. Even if it is just want to fit into that sexy full bikini you need to understand the possible risks and benefits of silicone prosthesis.

Having said all of these, there are very few patients who regret choosing silicone prosthesis for reconstruction and even less so for augmentations.

Thank you for reading this article, we hope that we have answered some of the common questions associated with silicone implants.
IMPORTANCE OF ONCOLOGY CARE PHYSICIANS IN CANCER SURVIVORSHIP

“WHAT NOW? WHAT HAPPENS AFTER MY CANCER IS IN REMISSION?”

ONCOLOGY CARE PHYSICIANS ARE DOCTORS WHO ARE TRAINED TO CARE FOR CANCER SURVIVORS, AND AS SUCH FORM AN IMPORTANT PART OF THE CANCER MANAGEMENT TEAM.

The value of oncology care physicians has been recognised internationally, and South Africa has recently started to appreciate the potential for improvement in patient care through the introduction of oncology care physicians. The improvement in screening and treatment of cancers has resulted in an increase in the number of cancer survivors, and the number of survivors is only set to increase even more over the next few years. This will result in a large number of patients who still need specialised care after their cancer has been treated, and not enough cancer specialists to adequately follow up and care for these patients.

We, as oncology care physicians, are in the perfect position to assist in the management of these patients from initial diagnosis right through to remission. We are often the first contact the patient has with a doctor, before the patient is referred to a specialist for further treatment of the cancer, and we continue to see the patient throughout their cancer treatment for the management of other medical issues. We are not only experienced in managing general chronic medical conditions, such as high blood pressure and diabetes, but we are also able to provide the specialised care that cancer survivors need.

CANCERS TEND TO BE MORE PREVALENT IN THE AGEING POPULATION, AND IT IS ALSO THIS POPULATION THAT HAS THE HIGHEST BURDEN OF CHRONIC MEDICAL CONDITIONS.

We are able to recognise how cancer and chronic medical conditions influence each other, and we are therefore able to provide the highest level of care to these patients, thereby improving their quality of life significantly. We are able to screen patients for recurrence of their cancer, as well as any
new cancers that may develop either spontaneously or as the result of a genetic mutation or the treatment they received for the initial cancer. We are also able to recognise and manage the long term and late effects of cancer and cancer treatment.

We can empathise with and adequately address the profound emotional, social and financial burden that cancer survivors bear once their cancer is in remission. Patients trust us to manage every other aspect of their health, and now as oncology care physicians, we are also able to guide them through the difficulties and challenges that a cancer diagnosis brings.

CANCER SURVIVORS NEED NEVER AGAIN ASK “WHAT NOW? WHAT HAPPENS AFTER MY CANCER IS IN REMISSION?”

I am an oncology care physician practising in the Fourways area. My practice is located at TimRon Health and Wellness Centre, 256 Church Street, Johannesburg North, Randburg. The centre is owned by two dentists, Drs Tim and Rona Struwig, who are available to attend to all dental problems, including those arising as a result of cancer and cancer treatment.

We also boast a qualified physiotherapist and life coach, Monique De Beer. She has a wealth of experience in working with cancer-related complications and has a great passion for working with cancer survivors. Our beautician, Robyn Crowther, is skilled in providing a number of aesthetic treatments, and is available to address any skin complications that may present after cancer treatment.

Please phone (011) 462 7292 to book an appointment at TimRon Health & Wellness Centre.

Inge Kriel: Oncology Care Physician, Milpark Breast Care Centre of Excellence. Correspondence: ingekriel84@gmail.com
Exercise techniques are used to specifically focus on different parts of the body. The simple/gentle exercises and techniques can be done in various sitting positions, standing or lying down (if fatigued). Sophrology helps you to cope with trauma, stress, tension, depression and anxiety more efficiently.

Existing & being practiced in Europe for over 55 years, Sophrology produces optimal health and wellbeing and has proven to be superior to other wellness initiatives.

Ishana Maharaj

WHAT IS SOPHROLOGY?

Sophrology is a wellbeing technique that comprises of various breathing techniques, simple and effective exercises, visualizations, meditation/mindfulness and many additional techniques added to it. These exercises are called “Dynamic Relaxation”, which is relaxation in movement.

IT IS A STRUCTURED, HIGHLY EFFECTIVE HOLISTIC PROGRAM THAT WORKS THE MIND, BODY AND SPIRIT SIMULTANEOUSLY. IT HARMONIZES/ACTIVATES/STIMULATES/REJUVENATES ALL CELLS OF THE BODY, ORGANS, GLANDS, SYSTEMS, BONES, MUSCLES AND SKIN.

SOPHROLOGY COMPRIZES OF THE 4 LEVELS BELOW.

Each level works different parts of the body and achieves various outcomes. The results achieved by each exercise may be different for every patient, as each individual is different. A patient does not have to do ALL levels to benefit from Sophrology.

Body/Breathing awareness, improve concentration, confidence, sleep, self-esteem, reduce stress/anxiety, activating skin cells

Mind/brain exercises, positive goals, achievements, focus on muscles, how 5 senses link to mind, transformation of mind/body/spirit

Explore inner/outer world, focus on bones/cell structures, emotional link of mind & body, control & manage emotions

Completion of phronic region, complete transformation, focus on organs, awareness/living of values, helps decision making

DISCOVERING THE CONSCIOUSNESS: ENLIGHTENMENT

Ishana Maharaj
Through his passion for Sophrology, it became known in the world. He delivered conferences at many medical symposiums and together with Pierre Schwar, created the Swiss Academy of sophrology. He trained the large sophrology schools in France and was the head of sophrology training for the Swiss Academy.

**THE 6 SYSTEMS**

In Sophrology, we divide the body into 6 systems which are neutral areas, each associated with particular parts of the body and particular functions within the body controlled by the nerve plexus, organs, cells, bones, muscles or endocrine gland/s associated with that system.

During a sophrology exercise, specific techniques are used to work down or up the body. One focuses on the information given from each major nerve plexus. It is more effective to focus on a small part of the body each time in stages, as it is easier to notice the physical sensations in more detail, than when focusing on the whole body at once.

**ORIGINATION**

Sophrology was a term created by Professor Alfonso Caycedo in 1960. Residing in Spain as a Neuropsychiatrist, he developed this method to improve the physical and mental health of people, without the use of medication.

HE IMPROVED THE LIVES OF DEPRESSED, ANXIOUS AND WAR TRAUMATIZED PATIENTS. SOPHROLOGY WAS DERIVED FROM THE GREEK TERMS SOS, PHREN AND LOGOS, MEANING “THE STUDY OF CONSCIOUSNESS IN HARMONY”.

Dr Raymond Abrezol was the main ambassador for sophrology in the world. He was instrumental in taking sophrology out of the purely medical environment and insisted that it was needed to be used as a “preventative method”. He coached the Swiss Ski Team to gold medals and directed Sophrology to top sports professionals.

**BELOW IS A DIAGRAM OF THE 6 SYSTEMS WHICH INCLUDES INFORMATION FOR THE PART/S OF THE BODY, ORGANS, AND ENDOCRINE GLAND/S CONTAINED IN EACH SYSTEM.**

1. **First System**
   - Head: Brain, eyes, nose, ears, mouth & jaw
   - Hypothalamus, pituitary & pineal glands

2. **Second System**
   - Neck, throat, shoulders, back of arms, back of hands & fingers
   - Thyroid & parathyroid glands

3. **Third System**
   - Chest, upper back, underside of the arms, palms of the hands, front of fingers
   - Thymus gland

4. **Fourth System**
   - Area between chest & navel, middle of back
   - Internal organs: liver, kidneys, stomach
   - Pancreas & Adrenal gland

5. **Fifth System**
   - Lower abdomen, lower back, hips, legs, feet & toes
   - Ovaries & testicles

6. **Sixth System**
   - Point of navel signifies the whole body
   - Endocrine System
Ishana Maharaj: Sophrology Practitioner - Having worked in the corporate world for over 18 years, I resigned as a Project Manager to relocate to Switzerland with my family, for a few years. During my time in Geneva, I discovered Sophrology, and was fascinated by its history, and widespread adoption in Switzerland, France, Spain and the UK over the last 55 years. Having studied Sophrology at a leading institution in Geneva, Switzerland, I personally experienced the benefits of this journey. Returning to my home in South Africa as a Sophrology Practitioner, being a Mum of 3 children (son-17yrs & twin girls 10yrs of age), I felt blessed with a “gift”. A special gift to share with people of South Africa. My ultimate passion is to create an awareness, help, support, share my knowledge and experiences of this phenomenal wellness technique, with people. As the first Sophrologist in Johannesburg, my practice resides in Eagle Canyon Business Centre, Eagle Canyon Estate, Honeydew. Correspondence: ishana@sophrology.co.za; www.sophrology.co.za; Cell: 0827994311.

SIX SYSTEMS

A TYPICAL SOPHROLOGY SESSION

For individual sessions, a once-off goal oriented questionnaire is completed by the patient. This is analyzed by the Sophrologist, so that exercises can be customized to suit your needs. The Sophrologist goes through specific exercise techniques and provides information that needs to be followed by the patient.

THE EXERCISE SESSION STARTS WITH A BREATHING TECHNIQUE, A FULL MINDFUL BODY SCREENING, TENSION RELEASE OF EACH SYSTEM, BREATHING AND EXERCISE TECHNIQUES. EACH EXERCISE TAKES 20 TO 30 MINUTES, WHICH CAN BE DONE DAILY OR THREE TIMES A WEEK. THERE IS NO TOUCHING DONE BY THE SOPHROLOGIST. A RECORDING OF EACH SESSION IS GIVEN TO THE PATIENT TO DO THEMSELVES. SOPHROLOGY CAN ALSO BE DONE WITH GROUPS, HOWEVER NO QUESTIONNAIRE IS DONE AND EXERCISES MAY BE CUSTOMIZED TO SUIT EACH GROUP.

WHY DO SOPHROLOGY?

Sophrology is widely used for Maternity, Corporate, Sport, Education, Rehab centre’s, Specific Clinics (e.g. trauma, cancer, HIV) and Hospitals. It’s simplicity and flexibility enables people to do it at any time, at any place, by anyone i.e. children and adults of all ages.

No medication is administered and there’s no interaction with current medication taken. This unique, phenomenal journey is fun, pleasurable and empowers an individual to take control of their own body, mind and wellbeing.

Stress and anxiety is experienced within all age groups and is increasing rapidly in society. Due to ongoing hectic lifestyles, we are not immediately aware of the impact it has on our mental, physical and emotional wellbeing.

Untreated, constant stress can result in serious health conditions, eg. high blood pressure, heart disease, insomnia, burnout, and a weakened immune system.

SOPHROLOGY IMPROVES THE QUALITY OF LIFE, TO ENSURE “LIFESTYLE SUSTAINABILITY”. THIS RESULTS FROM A “HOLISTIC TRANSFORMATION” OF THE BODY, MIND AND SPIRIT. A SUSTAINABLE LIFESTYLE, THAT ONLY YOU CAN CREATE AND MAINTAIN.
SURVIVORSHIP CARE
HELPING CANCER SURVIVORS FIND THEIR NEW NORMAL

Inge Kriel

A cancer diagnosis is devastating, not only for the patient, but for her family and friends as well. It is a life changing experience in every sense: physically, psychologically, socially and financially.

The patient is propelled through treatment (often comprising a combination of surgery, chemotherapy, radiation and endocrine therapy), and is left physically and emotionally drained afterwards. Active treatment is comprised of a series of rigidly scheduled appointments, with the patient having a clear idea of where to be and what to expect.

The post-treatment period often leaves the patient feeling isolated, unsure of what is normal, and unsure of what to expect. The patient does not know who to turn to for advice and reassurance and she is often scared to bug her busy oncologist with trivial complaints.

This is where survivorship care plays a crucial role in the post-treatment care of the cancer patient. Survivorship care guides the patient through the survivorship period, helping her to re-adjust to her new life after cancer.

GP-driven survivorship care ensures that the patient has an easily accessible healthcare practitioner who can reassure her that the new lump she is feeling in her breast isn’t a cancer recurrence and that the burning sensation in her hands and feet can be managed and doesn’t have to impair her ability to lead a normal life. Side effects from chemotherapy and radiation may present immediately, or only be apparent much later. A patient who is five years post-treatment might not realise that the symptoms she is experiencing may be a consequence of her cancer treatment, and as such she may not seek help for these symptoms.

Oncology care physicians take a detailed history and screen specifically for treatment-related side effects, so that any treatment-related issues can be addressed to improve quality of life. Adherence...
to endocrine therapy is often problematic for the breast cancer survivor as this treatment needs to be taken for up to ten years.

**THE PATIENT OFTEN DOESN’T UNDERSTAND THE VITAL IMPORTANCE OF THIS LIFE-SAVING TREATMENT, AND MAY CHOOSE TO STOP THE MEDICATION DUE TO NEGATIVE PERCEPTIONS AROUND THE SIDE EFFECTS.**

The patient may even erroneously attribute any symptoms she is experiencing to the endocrine therapy, even though there may be another underlying reason for her symptoms. Therapy, even though there may be another underlying reason for her symptoms.

Extensive counselling and regular follow up is often needed to change the patient's perception around the medication and address underlying symptoms, to ensure adherence.

The cancer survivor may have co-existing cardiovascular, respiratory and orthopaedic conditions. These conditions may exacerbate any side effects from the cancer treatment, and therefore the patient needs to be managed holistically to improve quality of life. A multidisciplinary approach is crucial for holistic care.

Oncology care physicians need to refer (as appropriate) to cardiologists, pulmonologists, gynaecologists, orthopaedic surgeons and other specialists, and allied health professionals such as physiotherapists and occupational therapists, to optimise the care of the patient.

She may have a diverse range of unique survivorship needs that require a team approach. Sexual dysfunction, for example, is a multifactorial complaint which has a significant negative impact on quality of life.

**THE CANCER SURVIVOR MAY NOT BE COMFORTABLE TALKING ABOUT THIS PROBLEM AND THIS THEREFORE REQUIRES A GENTLE APPROACH FROM MULTIPLE HEALTHCARE PROFESSIONALS, INCLUDING A WOMEN’S HEALTH PHYSIOTHERAPIST TO EVALUATE AND TREAT PELVIC FLOOR DYSFUNCTION.**

Screening for recurrence of the primary cancer and the development of new cancers, is an important part of survivorship care. Education around healthy lifestyle choices is pivotal to improve the overall health of the patient and decrease her risk of recurrence, while empowering her to take back control of her health and her life.

**SURVIVORSHIP CARE IS THE CANCER SURVIVOR’S SAFETY NET – THE SPACE WHERE SHE CAN DISCUSS EMBARRASSING SYMPTOMS, ASK SILLY QUESTIONS, GET EMOTIONAL SUPPORT AND BE RECOGNISED AS THE BEAUTIFUL BRAVE WARRIOR SHE IS**

**Inge Kriel** is an Oncology Care Physician, Milpark Breast Care Centre of Excellence. **Correspondence: ingekriel84@gmail.com**
Breast cancer survivors have unique needs after active cancer treatment. Hair loss, dry skin, brittle nails, burning and tingling in the hands and feet (peripheral neuropathy), and vaginal dryness are only some of the myriad afflictions that a survivor may need to deal with day-to-day.

These conditions are distressing, and can have a significant impact on a patient’s quality of life. Many breast cancer survivors do not seek help for these conditions, either because they feel that their complaints are too trivial or embarrassing to discuss with their oncologist, or they fear having to take more pills (with their own ensuing side effects). They also worry about any potential interactions any medication may have with their ongoing cancer treatment (for example tamoxifen).

LET’S FIRST CLARIFY WHAT A COMPOUNDING PHARMACIST IS, IN ORDER TO BE ABLE TO EXPLAIN HOW COMPOUNDING PHARMACY CAN BE USEFUL IN HELPING BREAST CANCER SURVIVORS DEAL WITH THEIR SURVIVORSHIP NEEDS.

The medication can then be administered to the patient through a variety of routes: oral, rectal, intranasal (through the nose), and transdermal (through the skin). The benefit of the transdermal mode of delivery is that many of the side effects of the oral route can be avoided, as the medication is absorbed directly through the skin and therefore bypasses the gut, liver and kidneys. Only a small amount of the drug is absorbed into the bloodstream. This is particularly important for cancer patients who may already have some degree of organ impairment due to the cancer or the cancer treatment. Postmenopausal symptoms are particularly worrisome for breast cancer survivors.

A COMPOUNDING PHARMACIST IS AN INDIVIDUAL WHO PERSONALISES A MEDICATION FOR A PATIENT BY MIXING UP INDIVIDUAL INGREDIENTS IN THE EXACT DOSAGE AND STRENGTH AS REQUIRED BY THE PATIENT.
Chemotherapy and endocrine therapy may launch a patient into early menopause, with all the accompanying side effects: irritability, dry skin, hot flushes and vaginal dryness. These symptoms can have an overwhelmingly negative effect on her overall quality of life, adding to concerns around body image, sexual function and fertility.

Oestradiol gels for vaginal dryness and gels to enhance orgasm, can significantly improve sexual function. Specialised skincare products can help to nourish dry skin. Brittle nails (often as a result of Herceptin), can be managed with Biotin capsules. Peripheral neuropathy after taxane-based chemotherapy can be particularly bothersome and may lead to balance disturbances. This can impact a woman’s ability to exercise, with a significant negative impact on her overall health and risk of cancer recurrence. A ketoprofen/gabapentin gel formulation can significantly improve symptoms of peripheral neuropathy.

The pharmacists then contact the patient and arrange for a quote to be sent through to the patient. The cost of the products range anywhere from R40 to R400, depending on the cost of the raw materials that need to be obtained to formulate the products. A small delivery fee is charged and the products are couriered directly to the patient, once the patient has made payment.

I then follow up with the patient to determine their response to the treatment. If response is sub-optimal, I would adjust the strength or dosage of the treatment and the pharmacists would then re-formulate the product according to my specific instructions.

I also obtain feedback from the patients regarding ease of application, as well as any other comments/criticism, and send this information through to the pharmacists, so that the products can be improved or adjusted accordingly.

This ensures that the patient remains adherent on the treatment, as she feels her specific concerns are being addressed. Women do not have to suffer debilitating side effects as a result of cancer and cancer treatment.

A range of personalised medications, tailor-made to suit a survivor’s unique needs, are available to manage side effects.

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LIFE WILL NEVER BE THE SAME AS BEFORE THE CANCER, BUT WE CAN HELP PATIENTS TO FIND THEIR NEW NORMAL AND LIVE A HAPPY, FULFILLING LIFE AFTER CANCER. WOMEN CAN ONCE AGAIN TAKE CONTROL OF THEIR LIVES, AND ALL THAT MAKE THEM WOMEN.
TRIPLE NEGATIVE BREAST CANCER AND IMMUNOTHERAPY

BERNARDO L. RAPOPORT

TRIPLE NEGATIVE BREAST CANCER

The many advances in the general understanding of breast cancer over the past few decades have led to better diagnostic methods and improved treatment modalities, including new chemotherapeutic agents and targeted therapies. Survival of breast cancer has been greatly improved as a result of these advances. Testing for hormone receptor status - oestrogen receptor (ER) and progesterone receptor (PR) as well as HER2 status are main factors determining treatment options for breast cancer. HER2+ breast cancer is a breast cancer that tests positive for a protein called HER2. HER2 is an important trans-membrane protein that influences the normal growth and survival of cells. Overall 15-20% of breast cancers can be classified as triple negative, indicating a type of cancer in which cells do not show cell-surface expression of any of the three major receptors (ER, PR and HER2).

WHILE TRIPLE NEGATIVE BREAST CANCERS (TNBC) ARE GENERALLY RESPONSIVE TO NEO-ADJUVANT CHEMOTHERAPY, THEY ARE USUALLY AGGRESSIVE AND ARE SHOWN TO BE ASSOCIATED WITH WORSE OVERALL SURVIVAL COMPARED TO HR+/HER2- PATIENTS. TRIPLE-NEGATIVE TUMOURS ARE ALSO ASSOCIATED WITH A GREATER RISK OF BRAIN OR LUNG METASTASES.

IMMUNOTHERAPY

Immunotherapy has become an important part of treating some types of cancer. Newer types of immune treatments are now being studied, and they’ll impact how we treat cancer in the future.

The main types of immunotherapy now being used to treat cancer include:

- Monoclonal antibodies (mAb): Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that...
can restore, enhance or mimic the immune system’s attack on cancer cells. Antibodies can be very useful in treating cancer because they can be designed to attack a very specific part of a cancer cell.

- **Immune checkpoint inhibitors:** These drugs basically take the ‘brakes’ off the immune system, which helps it recognize and attack cancer cells. The immune system has checkpoint proteins (such as programmed death and programmed death ligand 1 - PD-1/PDL-1 and Cytotoxic T lymphocyte associated molecule-4 - CTLA-4) that help keep it from attacking other normal cells in the body.

  Cancer cells sometimes take advantage of these checkpoints to avoid being attacked by the immune system. Checkpoint inhibitors have become an important part of the treatment of cancers like melanoma and non-small cell lung cancer. Unlike most other cancer drugs, these checkpoint inhibitors seem to be helpful against many different types of cancer.

- **Cancer vaccines:** Cancer treatment vaccines boost the immune system’s ability to recognise and destroy antigens (substances on the surface of cells that are not normally part of the body). They stimulate the immune system to recognise and destroy cancer cells that have these molecules on the surface.

- **Other, non-specific immunotherapies:** These treatments boost the immune system in a general way, but this can still help the immune system attack cancer cells.

**WHILE BREAST CANCER HAS NOT HISTORICALLY BEEN THOUGHT OF AS AN IMMUNOGENIC TUMOR, THERE HAVE BEEN A NUMBER OF OBSERVATIONS MADE OVER THE PAST DECADE THAT HAVE PROVIDED THE RATIONALE FOR INVESTIGATING IMMUNOTHERAPY AS A VIABLE THERAPEUTIC OPTION FOR TNBC.**

ER-negative breast cancers have a higher density of tumour infiltrating lymphocytes (TILs) than their ER-positive counterparts. The ability to profile breast tumours on a molecular level has led to two key observations: first, that programmed death ligand 1 (PDL-1) gene expression is significantly greater in TNBCs compared with non-TNBCs, and second, that a subset of TNBC tumours—the immunomodulatory subtype—is characterized by elevated expression of genes involved in T-cell function.

Furthermore, TNBCs are genomically unstable and have high rates of genetic mutations, which can in turn lead to neo-antigen presentation and induction of an immune response through activation of the cancer-immunity cycle.

Immune checkpoint inhibition has now been studied in several clinical trials in TNBC with encouraging results. In addition, the toxicity is manageable. Combination therapies are exciting, and hold the promise of building on the modest responses seen with anti-PD-1/PDL-1 monotherapy.

*Bernardo L. Rapoport* is a Professor in the Department of Immunology, Faculty of Health Sciences, University of Pretoria and Medical Oncologist in private practice in Johannesburg. He is in private practice at The Medical Oncology Centre of Rosebank Johannesburg, South Africa. Correspondence: Please contact the relevant sub-editor as well as cc the Editor-in-Chief for more information.
The Centre situated in the Netcare Waterfall City Hospital has been Internationally Accredited by the European Chapter of IFSO and provides training to surgeons, dieticians and nurses from hospitals countrywide who reside under the umbrella of Life Healthcare, Netcare and Mediclinic. Known Medical Aids only support patients and doctors who form part of a Centre of Excellence for Metabolic Medicine and Surgery in Hospitals that are accredited by the International Accredited Centre in Midrand.

The future for bariatric surgery looks exceptionally good as obesity is one of the chronic diseases that affects people all over the world. In 2015 out of 10 billion people globally, 2 billion were overweight or obese. This congress is an educational tool with regards to the sensitizing and changing of the misconceptions of obesity.

We foresee a growth in numbers at our next congress as more and more people realize that obesity has now even started to affect young adolescents - and drastic measures in educating the government, medical practitioners and the public are now needed.
The congress programme included a range of both international and local speakers, with the opening plenary lecture “Understanding the long-term efficacy of bariatric surgery on type 2 diabetes” delivered by Prof Philip Schauer (Professor of Surgery at the Cleveland Clinic Lerner College of Medicine and Director of the Cleveland Clinic Bariatric and Metabolic Institute).

The speaker for the Per Björntorp lecture “Why the DSS guidelines and STAMPEDE trial matters and what to do next” was Prof Philip Schauer (Professor of Surgery at the Cleveland Clinic Lerner College of Medicine and Director of the Cleveland Clinic Bariatric & Metabolic Institute).

The CEMMS speaker was Prof Tess van der Merwe who spoke on “New Data for SA”.

The presentations also included 2 webinars involving Prof Christopher Szabo who spoke on the topic “Understanding eating disorders” with the second “What the general practitioner needs to know” Chaired by Dr Andre Potgieter and featuring a range of speakers covering different topics: Mr David Goncalves: “Understanding the brittleness of the obese patient”, Dr Gert du Toit: “How to select the right patient”, Dr Andre Potgieter “How to identify possible complications” and Dr Irshaad Ebrahim: “Sleep apnea in the obese”.

A symposium hosted by Welch Allyn related to strategies for in-hospital care of bariatric patients and covered specific areas i.e. understanding the implications of obesity and challenges encountered by bariatric patients, recognising the institutional barriers to effective care and identifying readiness strategies which can help prevent injuries.

Included in the programme was an Ethics lecture by Prof Mervyn Mer and 2 lectures from Dr Heidi Lombaard “Anesthesia in bariatric surgery”, and Dr Gary Fetter “What does the bariatric outcome data show for Waterfall City Hospital?”. The Congress closed with a Round table discussion (moderated by Prof Tess van der Merwe) and comprising 2 sessions, each with multiple discussants and covering the topics of: Surgery and complications and Procedure selection

This congress would not have been such a success without the support and educational sponsorships from the prominent medical companies such as Netcare, Johnson & Johnson and Medtronic. Our sincere thanks also go to the companies in the medical environment who saw the enormous potential of using our congress to exhibit their products. Some of them are service providers in our ten Centres of Excellence for Metabolic Medicine and Surgery in South Africa

Prof. Philip Schauer

Prof Mervyn Mer

Dr Heidi Lombaard

Dr Gary Fetter

Tess van der Merwe is Honorary Professor and Researcher in the Department of Endocrinology, University of Pretoria; CEO of the 11 Centres for Metabolic Medicine and Surgery of South Africa (CEMMS)(SA); Director of the Waterfall City Hospital Metabolic Medicine and Surgery Centre Research group and is a full time clinician at this hospital.

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INSTRUCTIONS TO AUTHORS

South African Women’s Health publishes original contributions that relate to the health of South African women. The aim of the publication is to promote best practice for optimal care.

The following types of content are published, noting that the list is not prescriptive or limited and potential contributors are welcome to submit content that they think might be relevant but does not broadly conform to the categories noted:

LETTERS TO THE EDITOR
- Novel experiences
- Response to published content
- Issues

FOCUS ON
- Related to a specific area of interest
- Related to service development
- Related to a specific project
- A detailed opinion piece

REPORTS
- Related to events e.g. conferences, symposia, workshops

NEWS
- Academic Departments e.g. graduations, promotions, appointments, events, publications

ANNOUNCEMENTS
- Congresses, symposia, workshops
- Publications, especially books

The format of the abovementioned contributions does not conform to typical scientific papers. Contributors are encouraged to write in a style that is best suited to the content. There is no required word count and authors are not restricted, but content will be subject to editing for publication. References may be noted in text and included in a references section. If not published with content, they will be noted as available from the author/designated author where there are multiple authors. All content should be accompanied by a relevant photo (preferably high resolution – to ensure quality reproduction) of the author/authors as well as the event or with the necessary graphic content.

Please note a brief biography of the author/authors must accompany content, including discipline, current position, notable/relevant interests and an email address. Contributions are encouraged and welcomed from the broader mental health professional community i.e. all related professionals, including industry. All submitted content will be subject to review by the editor-in-chief, and where necessary the advisory board.

All content should be forwarded to the Editor-in-chief, Carol Benn - drbenncarol@gmail.com

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