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ORIGINAL ARTICLE – BREAST ONCOLOGY

Robotic Prophylactic Nipple-Sparing Mastectomy with Immediate Prosthetic Breast Reconstruction: A Prospective Study

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ABSTRACT

Background. Robotic nipple-sparing mastectomy (RNSM) could be a significant advancement in the treatment of breast cancers and prophylaxis because the mastectomy is performed without leaving any scar on the breast. The aim of this study was to assess the feasibility and the safety of RNSM with immediate prosthetic breast reconstruction (IPBR).

Methods. In this prospective study, RNSM with IPBR was offered to patients with breast cup size A, B or C and ptosis grade ≤ 2. In case of oncologic surgery, RNSM was proposed only if the tumor was located more than 2 cm away from the nipple-areola complex (NAC) and if postoperative radiation was not indicated. In case of prophylactic surgery, RNSM was proposed only if a high-risk genetic mutation had been identified. The primary endpoint was the rate of skin or NAC necrosis. The rate of conversion to open technique, the duration of the procedure, and postoperative complications were also analyzed.

Results. Sixty-three RNSM with IPBR were performed in 33 patients. There were no cases of mastectomy skin flap or NAC necrosis. We had to convert to an open technique in one case (1.6%). Three infections occurred (4.8%), one leading to implant loss (1.6%). No other major complications were observed.

Conclusions. Preliminary data attest to the feasibility, the reproducibility, and the safety of this approach. However, long-term data are needed to confirm the oncological safety and the esthetic stability of the result.

Trial registration identifier NCT02673268.

Nipple-sparing mastectomy (NSM) is the latest advance for the treatment of selected breast cancers and prophylaxis.[1–4] An increasing number of women are choosing mastectomy for risk reduction.[3,4] Consequently, the demand to improve cosmetic results in breast reconstruction is rising steadily.[5,6]

When planning an NSM, incision placement is a critical decision. Incision location may affect the rate of skin or nipple-areola complex (NAC) necrosis, because any skin incision might compromise the vascularization of the skin flaps.[7] Some kinds of incisions also may lead to NAC malposition or distortion.[8] In addition, any visible scar on the breast will negatively impact the result.

The endoscopic approach to breast surgery provides more cosmetically acceptable incisions while enhancing surgical exposure.[9–11] However, technical limits have prevented this technique from being adopted in clinical practice. The two-dimensional endoscopic in-line camera produces an unsuitable optical window, whereas the manual control of rigid-tip instruments limits the internal mobility around the curvature of the breast.

Toesca et al. were the first to describe the surgical technique of robotic NSM (RNSM) with immediate prosthetic breast reconstruction (IPBR).[12,13] Instruments with motion-scaling, high-resolution, three-dimensional optics,

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tremor elimination, and enhanced precision with 7-degrees of freedom have allowed the limitations experienced with the endoscopic approach in breast surgery to be overcome.[12,13]

We have assessed the technical feasibility of RNSM through lateral axillary incisions on cadavers.[14] Because the da Vinci robotic Surgical System® currently does not have CE mark or FDA clearance for NSM indication, the procedure of RNSM had to be explored in the context of a prospective study. The purpose of this prospective study was to assess the feasibility and safety of RNSM with IPBR based on the first 63 consecutive procedures performed in our institution.

PATIENTS AND METHODS

Patient Selection

Patients were prospectively included from November 2015 to July 2017. The same surgeon performed all procedures. Patients had to meet the following criteria: breast cup size A, B, or C (based on bra size) and ptosis grade ≤ 2 (Regnault ptosis scale) (otherwise a skin-reducing, nipple-sparing mastectomy was indicated); between ages 18 and 70 years; and Eastern Cooperative Oncology Group (ECOG) score 0 or 1. In case of oncologic surgery, RNSM was offered if the tumor was located more than 2 cm away from the NAC. In case of prophylactic surgery, RNSM was proposed if a high-risk genetic mutation had been identified.

Patients were not included if postoperative radiation therapy was indicated. Patients with history of breast surgery or breast radiation therapy, heavy smokers (more than 20 cigarettes a day), and patients with uncontrolled diabetes mellitus were not eligible for the study. Before the procedure, every patient provided signed informed consent for RNSM with IPBR according to the established regulations.

Design

This single-arm, monocentric descriptive study was performed in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki. The institutional review board at Gustave Roussy, an ethics committee, and health authorities approved the study protocol. The initial goal of the study was to assess the feasibility of RNSM with IPBR on 35 consecutive patients, which was further amended to include 80 patients. As per the amended protocol, the primary endpoint was the rate of major necrosis (mastectomy skin flap or NAC necrosis that requires surgery). Secondary endpoints included the conversion rate to open technique, the duration of surgery, and the rate of postoperative complications: minor necrosis (mastectomy skin flap or NAC necrosis that only requires local wound care), hematoma, seroma, infection, implant exposure, implant loss, implant malposition, and the duration of postoperative drainage.

Follow-up visits were scheduled at 1, 3, 6, and 12 months after the procedure. Patients completed a Breast-Q questionnaire before and 12 months after the procedure. They also completed a satisfaction questionnaire (assessing amongst other things the esthetic result) at 6 months and 12 months after the procedure.

An independent data monitoring committee (IDMC) was established for this feasibility study. The protocol is available upon request.

Surgical Technique

All procedures were performed with the da Vinci® Xi™ (Intuitive Surgical®, Sunnyvale, CA). A lateral-thoracic approach is associated with a high vertical scar of 3–5 cm, located within the footprint of the bra, with a subcentimeter vertical scar, located 8–9 cm below the previous incision. These incisions are located 6–7 cm posterior from the lateral-mammary fold. Rather than being left exposed in a visible area, the scars are hidden by and under the patient's arm (Supplemental Figure 1). Mastectomy and reconstruction by prosthesis were performed by using this approach. The higher scar enables the operator to introduce two trocars: to externalize the gland at the end of the intervention; and to introduce the prosthesis allowing for immediate breast reconstruction. The lower scar is used to insert the third trocar and to externalize the drain.

In the operating room, the patient was placed in flat supine position with the robot at her head. To reduce the risk of brachial plexus injury, the procedure begins with the arm at 90 degrees abduction. A 2-g dose of cefazolin was given 30 min before the incision. Infiltration with a saline solution containing 1 mg/mL of adrenaline was used to reduce bleeding and to facilitate subcutaneous dissection of the gland. Subcutaneous dissection was then performed as far as possible with scissors. Before inserting ports, we ensured that dissection was confluent between the two incisions to allow insertion of the instruments under endoscopic vision. Then, the arm was placed above the head with internal rotation and 90° abduction to reduce the conflicts between the arm of the patient and the robot. The upper incision was closed, and three 8-mm diameter ports were inserted and fixed with stitches to the skin incision. Robot docking was guided by the target sign, which had to be aligned both with the skin incision and the nipple (Supplemental Figure 2). One port was connected to the gas insufflator to keep a constant pressure of 8 mmHg during the working process. Carbon dioxide insufflation created an adequate working space for the robot (Supplemental Figure 3). The 30° camera (Intuitive Surgical®, Denzlingen, Germany) was introduced first in the middle port to allow non-traumatic insertion of the instruments under endoscopic vision. Dissection was performed with monopolar-curved scissors (Intuitive Surgical®, Sunnyvale, CA), whereas traction, counter-traction, exposure, and cauterization were performed by using bipolar grasping forceps (Intuitive Surgical®, Sunnyvale, CA). Subcutaneous dissection of the gland was completed in a lateral to medial direction, up to the limits of the gland. Then, the gland was separated from the pectoralis major muscle in a lateral to medial direction (Supplemental Figure 4).

The robot was undocked, the ports were removed, and the patient arm was placed back on the surgical armrest. Thereafter, the gland was extracted en bloc through the largest incision and sent for pathological examination. A 5-cm incision was large enough to remove a C-cup mastectomy specimen. We never had to extend the incision to remove the gland. A drain was placed through the inferior infracentimetric scar. The anatomical implant (Eurosilicone, Meless, France or Allergan, Inc., Irvine, CA or Mentor, Irvine, CA) was inserted in a prepectoral position. Finally, the implant pocket was closed laterally with two or three stitches between the skin and the thoracic wall to avoid any secondary malposition of the prosthesis.

Statistical Analysis

Categorical variables are summarized in frequency tables, with the counts and percentage of patients in each category. For continuous variables, summary statistics include number of patients, mean and 95% confidence interval, median, minimum and maximum values (range). Ninety-five percent confidence intervals (95% CI) for proportions were computed using the binomial approximation (or Wilson's method).

RESULTS

Patients

A total of 33 women underwent 63 RNSM with IPBR between December 2015 and July 2017 (Table 1). Only one patient underwent a therapeutic RNSM (ductal carcinoma in situ). A sentinel node biopsy was performed using the same incision and was negative. All other RNSM were performed for breast cancer risk reduction. One occult lobular carcinoma in situ was found in a mastectomy specimen. The weight of resected tissue ranged between 78 and 330 g. Breast reconstruction was performed exclusively with implants. Eight patients had a two-stage reconstruction at the beginning of the study, whereas the others had a direct-to-implant reconstruction. We decided to switch to a direct-to-implant reconstruction because we gained confidence with the technique. Definitive implant size ranged between 225 and 440 mL (median 312.5 mL). At the time of database freeze (September 2017), median follow-up was 9 months. Regarding patients' satisfaction, data are not yet available. Appearance of RNSM is shown in Figs. 1, 2 and 3 and Supplemental Figures 5–18.

Necrosis and Conversions

At day 21 after surgery, there were no cases of major/minor mastectomy skin flap or NAC necrosis, leading to an estimated necrosis rate of zero (0/63 RNSM, 95% CI 0-6%).

Only one procedure (1.6%, 95% CI 0.3–8.5%) was converted to an open technique because of bleeding from an internal mammary perforator that could not be controlled endoscopically. In this case, the patient received an additional incision in the inframammary fold. Bleeding was easily stopped under direct vision using this inframammary incision, and reconstruction was then performed in a conventional manner.

Duration of Surgery

Summary statistics of the duration by breast of RNSM with IPBR procedures are provided in Fig. 4. The duration of surgery has decreased over time. The entire procedure currently lasts for approximately 85 min.

Postoperative Complications

Three infections occurred (4.8%, 95% CI 0–13.3%). Two infections were managed with revision surgery to wash the implant pocket and to replace the implant. One infection unfortunately led to implant loss (1.6%, 95% CI 0–6%). We also observed one common peroneal nerve neurapraxia, which resolved spontaneously and had probably arisen because of patient malpositioning. One implant rotation also occurred. No other complication was observed. Drains were removed between the fourth and tenth postoperative day (median: 6 days). Patients were discharged once the drains had been removed. No hematoma or seroma have been reported so far.

TABLE 1 Patient characteristics ($N = 33$) and mastectomy characteristics ($N = 63$)

Age, years, median (range)	37 (24–52)
BMI, kg/m^2, median (range)	20.9 (17.6–30.1)
Chest size, number of patients (%)	
80 cm	2 (6.1)
85 cm	10 (30.3)
90 cm	18 (54.5)
95 cm	3 (9.1)
Cup size, number of patients (%)	
A	3 (9)
B	24 (73)
C	6 (18)
Regnault classification of ptosis, number of patients (%)	
0	20 (63)
1	5 (16)
2	5 (16)
3	1 (3)
4	1 (3)
Missing	1 (3)
Genetic mutation, number of patients (%)	
BRCA 1	22 (66.7)
BRCA 2	11 (33.3)
Smoking status, number of patients (%)	
Smoking (< 20 cigarettes/day)	2 (6.2)
Ex-smoker	1 (3.1)
Missing	2 (6.2)
Diabetes	0
Hypertension	0
Adjuvant hormonal treatment, number of patients (%)	
No	30 (91)
Yes	3 (9)
Menopausal status, number of patients (%)	
Pre	30 (91)
Post	3 (9)
Indication, number of RNSM (%)	
Prophylactic mastectomy	62 (98.4)
Therapeutic mastectomy	1 (1.6)
Breast cancer on the mastectomy specimen, number of RNSM (%)	
Yes	2 (3.2)
No	61 (96.8)

DISCUSSION

The purpose of our study was to assess feasibility of RNSM with IPBR. No case of necrosis occurred. We had only one case of conversion to open technique out of 63 procedures (1.6%), which was the result of uncontrolled bleeding.

The reproducibility and safety of this procedure have been illustrated by the low conversion rate (1.6%) and complications rate of this preliminary study. However, our technique differs from that described by Toesca et al.[12,13] First, we chose to perform the procedure in a flat supine position with the arm above the head, with internal rotation and 90° abduction, whereas Toesca et al.[12,13] usually leave the arm along the body. We had no complication related to the position of the arm. This position allows the robotic arms to move freely around the operative area without any conflict with patient's arm. Moreover, the scar may be placed more posteriorly. This makes it less visible with movements of the arm and, more importantly, enables introduction of the instruments further from the operative area, which facilitates dissection in the outer quadrants.

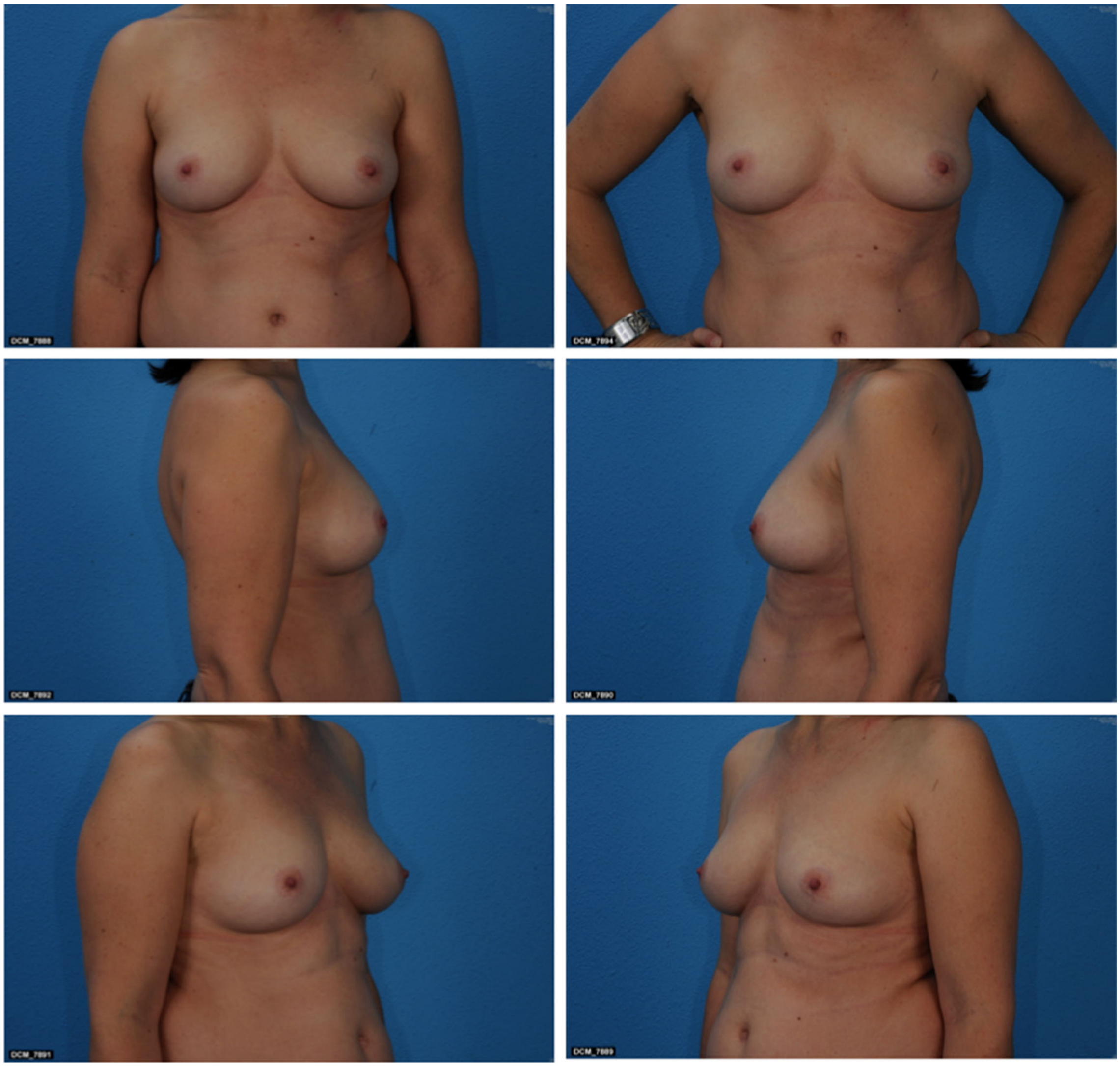

FIG. 1 Preoperative photographs of the 12th patient

Second, we decided to use two different incisions instead of one. A single-port robotic surgical system is unfortunately not yet available. Even though the da Vinci Xi® Surgical System may be used in combination with a monoport device; the dissection is not optimal as conflicts between robotic arms may happen.[12,13] Moreover, this approach requires use of a monoport device to maintain the right pressure in the pneumocavity, which significantly increases costs. Thus, before a single-port robotic surgical system becomes available, we prefer to add an additional infracentimetric scar, which facilitates the dissection. This infracentimetric scar is also used for the drainage.

Indeed, from a technical point of view NSM may be difficult to perform with the open technique owing to the small incision. The mastectomy skin flap might be damaged by the retractors or because of inadequate surgical exposure. The other risk is of performing an incomplete mastectomy. The endoscopic approach tried to solve such technical limitations while providing a more acceptable scar.[9] However, the manual control of a two-dimensional in-line endoscopic camera with limited internal mobility produces an inadequate optical window around the curvature of the breast. The rigid-tip instruments also are inadequate to work along the curvature of the breast. Such technical limits have prevented the endoscopic technique from being adopted in clinical practice. Compared with the endoscopic approach, the use of the da Vinci Xi® offers many advantages. The three-dimensional camera, which offers a tenfold magnified view of the operating field, facilitates the dissection, specifically in the crests of Duret plane, which is critical to avoid any post-operative skin or NAC necrosis. Moreover, motion scaling, tremor abolition, and the 7 degrees of freedom of motion at the tips of the robotic instruments enhance precision while

FIG. 2 Three-month postoperative photographs after bilateral robotic nipple-sparing mastectomy (RNSM) with immediate prosthetic breast reconstruction (IPBR)

also facilitating dissection along the curvature of the breast. Furthermore, carbon dioxide insufflation replaces the retractors used in the open technique and might be less invasive.

Despite these obvious technical advantages, the value of robotic surgery is debated in various specialties and its cost-effectiveness has been questioned.[15–17] In a large hospital with intensive robot use in various specialties, the additional costs of this new procedure are the additional operating room time and the costs of the instruments.[18,19] We observed a sharp reduction of the duration of surgery during the learning curve. The whole procedure of RNSM with IPBR currently lasts for approximately 85 min. This significant reduction of operating time may partially overcome the issue of operating room efficiency. Moreover, the additional costs of RNSM must be measured against postoperative savings. We are planning to compare the rate of skin and NAC necrosis between RNSM and the conventional technique in a head-to-head comparison study. Because there is no skin incision on the breast that may potentially interrupt the vascularization of the mastectomy skin flap, and because no retractor is used, one can assume that this risk should be reduced in comparison to open technique. A cost-effectiveness analysis is currently underway to assess the additional costs of the procedure compared with conventional NSM.

CONCLUSIONS

Preliminary data from more than 60 procedures attest to the feasibility, reproducibility, and safety of robotic nipple-sparing mastectomy. Advantages of this technique include a minimally invasive approach through a shorter and more acceptable scar and greater respect for the vascularization

FIG. 3 Three-month postoperative photographs after bilateral robotic nipple-sparing mastectomy (RNSM) with immediate prosthetic breast reconstruction (IPBR). Rather than being left exposed in a visible area, the scars are hidden by and under the patient's arm

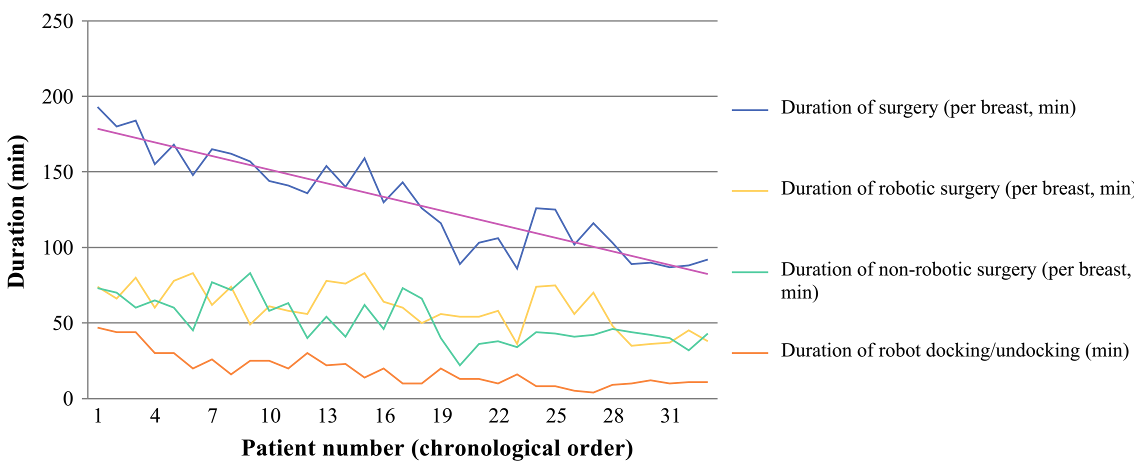

FIG. 4 Learning curve. The duration of surgery has decreased over time. The whole procedure of robotic nipple-sparing mastectomy with immediate prosthetic breast reconstruction currently lasts for approximately 85 min

of the mastectomy skin flap. However, long-term data are needed to confirm the reduced rate of skin and NAC necrosis compared with the open technique, the oncological safety, and the esthetic stability of the result.

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