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The learning curve of robotic nipple sparing mastectomy for breast cancer: An analysis of consecutive 39 procedures with cumulative sum plot

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A B S T R A C T

Background: The preliminary experience and learning curve of robotic nipple sparing mastectomy (R-NSM) in the management of breast cancer were analyzed and reported.
Methods: The medical records of patients who underwent R-NSM for breast cancer during the period of March 2017 to June 2018 were collected from the same surgeon in a single institute. Data on clinicopathologic characteristics, type of surgery, method of breast reconstruction, and operation time were prospective collected. Learning curve of R-NSM was evaluated and analyzed by the cumulative sum (CUSUM) plot method.
Results: A total of 39 consecutive R-NSM procedures from 35 patients were analyzed. The time needed for “docking”, “R-NSM”, and “R-NSM and immediate prosthesis breast reconstruction (IPBR)” decreased after cases experience accumulated, and in mature phase procedures could finished within 10 min, 100mins, and 240 min, separately. In CUSUM plots analysis of learning curve, the cases needed to decrease operation time for “docking”, “R-NSM”, and “total time for R-NSM and IPBR” were 13th, 13th, and 12th procedures separately. Mastectomy weight and lymph node metastasis were factors related to operation time. The rate of total nipple areolar complex necrosis for R-NSM was 0%. One (2.9%, 1/35) R-NSM procedure was found to have positive margin involved in the final pathologic check-up. No implant loss, or local recurrence was observed during a mean follow-up of 8.6 ± 4.5 (1.3–16.7) months.
Conclusion: From our preliminary experience, R-NSM and IPBR (or R-NSM alone) is a safe procedure, and the operation time needed significantly decrease after cases experience accumulated.
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Introduction

Robotic surgery, which incorporated 3-dimensional imaging system and flexibility of robotic arm and instruments, had been growingly used in different field of surgeries [1–4]. Robotic nipple sparing mastectomy (R-NSM) [5–10], which introduce *da Vinci* surgical platform through a small axillary wound to perform nipple sparing mastectomy (NSM) with (or without) immediate breast reconstruction (IBR), was reported to have potential to overcome the technique difficulty of endoscopic assisted nipple sparing mastectomy (E-NSM) [11–15] and showed promising cosmetic outcome [10].

Since 2015 when Toesca et al. [6,7] first proposed the technique of R-NSM, this new type of NSM raised the interests of incorporate robotic surgery in the management of breast cancer. Compared with conventional NSM, R-NSM was criticized with prolong operation time and increase medical cost [5,7,8,10]. Despite these limitations, persistent growing number of R-NSM performed in the world was observed [5,7,8,10]. Its application in the management of breast cancer or risk reducing prophylactic mastectomy is expected to be increased after more surgeons familial with this technique.

Learning curve is a concept that after repeat practice, surgeon could be familial with the operation and decrease the operation time [16–18]. The extra-time for docking of robotic surgery and time-cost necessary to complete the R-NSM was frequently criticized [5,7,8,10]. From previous reported series, the time for docking and completion of R-NSM was decreased after cases experience accumulated [5,7,8,10]. However, most of these experiences were derived from prophylactic mastectomy [8], when axillary surgery was not needed, or in small to medium sized breast (mastectomy specimen weight less than 300 gm) [7,8]. Rare study focusing on the learning curve of robotic mastectomy in the management of breast cancer was available.

In this study, we report the preliminary experience of R-NSM in the management of breast cancer and analyze the learning curve from the same surgeon in a single institute. The cumulative sum (CUSUM) method was used for the learning curve analysis of R-NSM in the management of breast cancer. Potential factors affecting operation time needed for R-NSM were also evaluated.

Materials and methods

Patients

Patients received R-NSM from March 2017 to June 2018 were searched from our robotic breast surgery database at Changhua Christian Hospital (CCH), a tertiary medical center in Taiwan. The data collected included clinicopathologic characteristics of patients, type of mastectomy, method of breast reconstruction, operative time, blood loss, hospital stay, complications, recurrence, and survival status at last follow-up. All data were collected by chart review by specially trained nurses and were confirmed by the principle investigator (HWL). The study was approved by the Institutional Review Board of the Changhua Christian Hospital (CCH IRB No.: 170806). Written informed consent to the use of clinical records was obtained from each participant. This current report includes photos of several patients, and they had agreed and signed the consent for publication of their pictures. The data reported in the current analysis also include the patient data reported in the earlier publications [5,10,19].

During the study period, a total of 41 robotic breast surgeries were performed in 35 female breast cancer patients, including 6 patients with bilateral disease. Among these 41 robotic breast procedures, 39 were R-NSM related. To evaluate the learning curve of R-NSM, these 39 R-NSM procedures were analyzed.

The inclusion criteria for R-NSM included early stage breast cancer (ductal carcinoma in situ (DCIS), stage I, II or IIIA), a tumor size less than 5 cm, no evidence of multiple lymph node metastasis, and no evidence of nipple, skin or chest wall invasion. Patients for whom R-NSM was contraindicated included those with apparent NAC involvement, inflammatory breast cancer, breast cancer with chest wall or skin invasion, locally advanced breast cancer, breast cancer with extensive axillary lymph node metastasis (stage IIIB or later), and patients with severe co-morbid conditions, such as heart disease, renal failure, liver dysfunction, and poor performance status as assessed by the primary physicians. Women with large (breast cup size larger than E or breast mastectomy weight >600 gm) and ptosis breast are not good candidate for R-NSM and IBR with Gel implant due to technique difficulty and sub-optimal cosmetic outcome. The inclusion and exclusion criteria were based on those reported previously [5,11–13,16,17].

Robotic nipple sparing mastectomy (R-NSM) technique

The techniques of R-NSM used in current study has been reported in previous studies [5,10]. Briefly, the patient was placed in the supine position and the arm was abducted 90°. A physiological saline solution containing lidocaine 0.05% and epinephrine 1:1,000,000 was injected subcutaneously to minimize bleeding. Then an approximately 2.5–5 cm oblique axillary incision (skin incision length depend on the size of the breast to be removed) was made over the extra-mammary region, and axillary lymph node surgery was performed if indicated.

After placement of the single port (Glove Port, Nelis, Gyeonggi-do, Korea, Fig. 1b), carbon dioxide (CO_2) was inflated with air pressure kept at 8 mm Hg to create space for mastectomy [5,6,10,15]. The operating side shoulder was elevated to 30° with draping and tilting to contralateral side to prevent conflict between the operating table and docking of robotic surgery system. Then robotic side cart (da Vinci, Intuitive Surgical, Sunnyvale, Calif.) is positioned posterior to the patient with the two robotic arms and the endoscope extending over the patient in proximity to the ports. In this position, the arms are aligned with the plane of the breast, nearly parallel to the floor, and the ports are docked to the robotic arms.

Then the operation was shifted to *da Vinci Si* (Intuitive Surgical, Sunnyvale, CA) robotic platform with operating surgeon controlled at the console (Fig. 1c). All the R-NSM cases reported in current study were carried out by the same surgeon (HWL). We use a 30° 12-mm-diameter camera (Intuitive Surgical, Denzlingen, Germany) in the upper port to prevent collisions of other instruments. Dissection was carried out with an 8 mm monopolar scissor (Intuitive Surgical, Sunnyvale, CA) used on the right robotic arm. Traction and counter-traction, along with maintaining exposure and stretching out the tissue was carried out with 8 mm prograsp forceps (Intuitive Surgical, Sunnyvale, CA) fitted on the left robotic arm. The location of scissor and prograsp in right or left arm could be adjusted during operation for performing the dissection and completion of mastectomy.

The dissection started from the superficial skin flaps in all quadrants. To facilitate skin flap dissection, tunneling technique was applied [5,10,12,13,17], and the septa between the skin flap and parenchyma were dissected using monopolar scissors. Then sub-nipple biopsy (Fig. 1d) was performed to detect occult cancer beneath the nipple areolar complex (NAC) [10,12,20]. After completion of superficial skin flap dissection, the peripheral and posterior dissection was carried out by pulling breast tissue to create a sufficient working space. Posterior dissection was performed by detach breast tissue from pectoralis major muscle and perforators were clearly identify. After the completion of dissection, the entire breast specimen was removed through the axillary

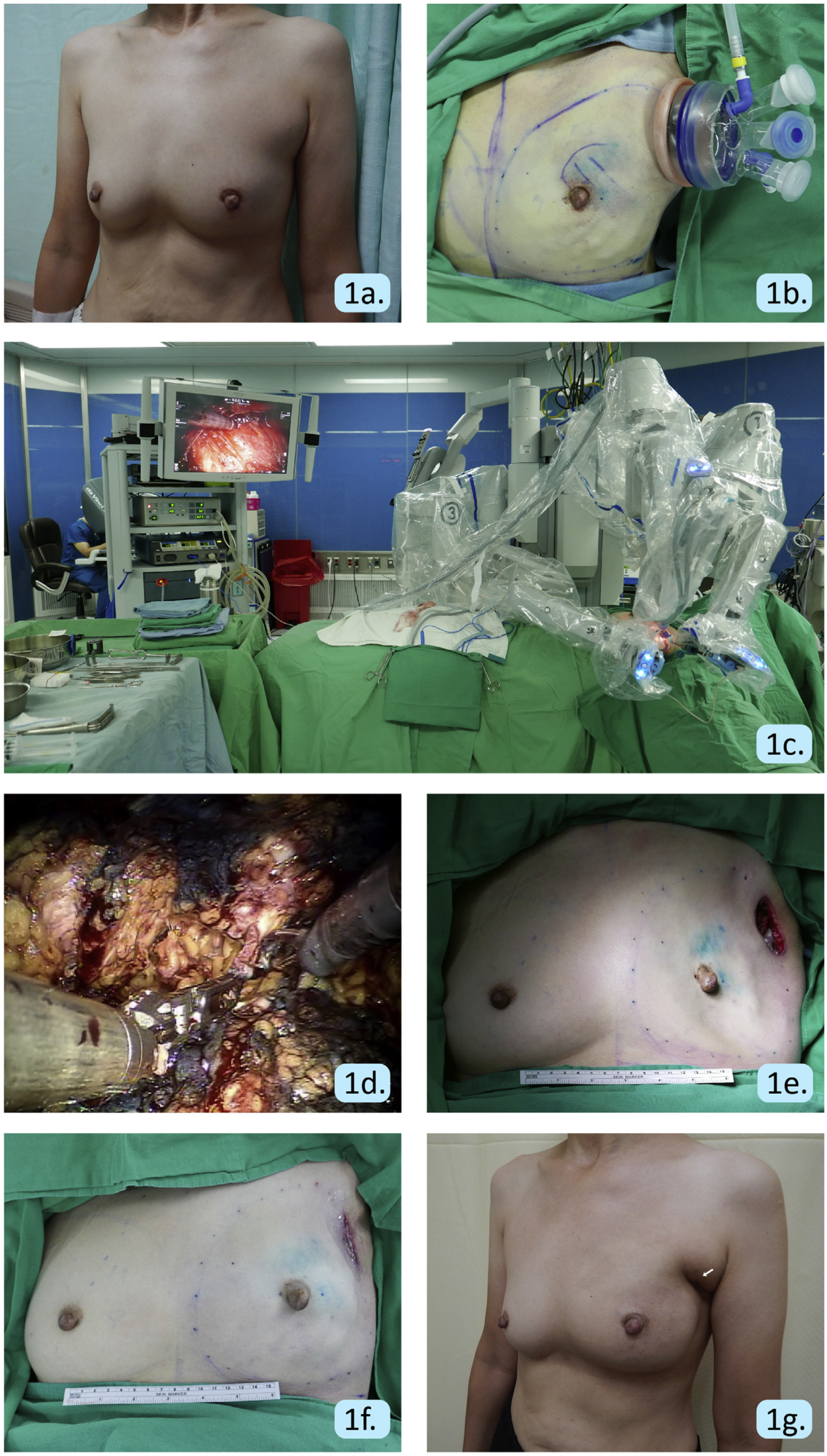

Fig. 1. Pictures illustrated robotic nipple sparing mastectomy (R-NSM) with immediate prosthetic breast reconstruction (IPBR). (a) Pre-operative view of 53 y/o female with left breast cancer selected for R-NSM and IPBR. (b) After sentinel lymph node biopsy, single port (Glove Port, Nelis, Gyeonggi-do, Korea) was inserted over the axillary wound, carbon dioxide (CO2) was inflated with air pressure kept at 8 mm Hg to create space for mastectomy. (c) Picture illustrated operation during R-NSM: the setting of robotic side cart (da Vinci, Intuitive Surgical, Sunnyvale, Calif.), and operating surgeon controlled the da Vinci Si surgical system at the console. (d) Picture illustrated operation during R-NSM: subnipple biopsy was performed to detect occult cancer invasion of the nipple areolar complex. (e) Picture represented of immediate post-mastectomy before reconstruction, the wound was small and hidden in the inconspicuous axilla region. (f) Immediate post-breast reconstruction outcome result front view. Cohesive Gel implant used for breast reconstruction was inserted from axillary wound and left in the sub-pectoral muscular pocket. (g) Post-operative 7 months lateral view. Bilateral breast was symmetry and nipple was well perfused. The wound was small and hidden in the inconspicuous axilla region.

Table 1
Clinicopathologic characteristics of patients receive robotic nipple sparing mastectomy for breast cancer.

All Robotic breast surgeries	N = 41		
Nipple sparing mastectomy	39		
Single	27		
Therapeutic	26	Gel implant reconstruction	24
		LD flap reconstruction	2
CPM	1	Gel implant reconstruction	1
Bilateral	12		
Therapeutic	6	Reconstruction	2
		No reconstruciton	4
Therapeutic + CPM	6	Reconstruction	2
		No reconstruciton	4
Partial mastectomy	2	LD flap reconstruciton	1
		Omentum flap reconstruciton	1

R-NSM	N = 39	
Age (year)	49.8 ± 9.9	(28.2–71.6)
Location		
Right	19	(48.7%)
Left	20	(51.3%)
Single/Bilateral	27/6	(69.2%/30.8%)
Sonogram tumor size (cm)	2.68 ± 1.2	(0.62–5.6)
Pathology tumor size (cm)		
Invasive	2.41 ± 2.9	(0.1–15.0)
In situ	2.12 ± 1.2	(0.8–3.7)
Clinical stage (NA = 7)		
Tis	10	(31.3%)
I	3	(9.4%)
IIA	14	(43.8%)
IIB	3	(9.4%)
IIIA	2	(6.3%)
Pathologic stage (NA = 5)		
Tis	10	(29.4%)
I	8	(23.5%)
IIA	9	(26.5%)
IIB	3	(9.4%)
IIIA	4	(12.5%)
Lymph node metastasis		
No	28	(71.8%)
Yes	11	(28.2%)
Lymph node stage		
N0	28	(71.8%)
N1	7	(17.9%)
N2	4	(10.3%)
Multi-centric/multi-focal lesion		
Yes	5	(12.8%)
No	34	(87.2%)
Margin status		
No involved	38	(97.4%)
Involved	1	(2.6%)
Grade (NA = 12)		
I	7	(25.9%)
II	16	(59.3%)
III	4	(14.8%)
ER (NA = 7)		
Positive	31	(96.8%)
Negative	1	(3.1%)
PR (NA = 8)		
Positive	20	(64.5%)
Negative	11	(35.5%)
HER-2 (NA = 15)		
Overexpression	2	(8.3%)
Negative	22	(91.7%)
Ki-67 (NA = 17)		
<14%	16	(72.7%)
>14%	6	(27.3%)
Subtype (NA = 9)		
Luminal A	23	(76.7%)
Luminal B1	5	(16.7%)
Luminal B2	1	(3.3%)
HER-2 type	1	(3.3%)
TNBC	0	(0%)
Lymph node surgery		
SLNB only	25	(64.1%)
SLNB then ALND	7	(17.9%)

Table 1 (*continued*)

R-NSM	N = 39	
ALND	1	(2.6%)
No surgery	6	(15.4%)
Breast reconstruction		
Gel implant	29	(74.4%)
LD flap	2	(5.1%)
No reconstruction	8	(20.5%)
Adjuvant treatment		
Endocrine therapy		
Yes	25	(64.1%)
No	14	(35.9%)
Chemotherapy		
Yes	11	(28.2%)
No	28	(71.8%)
Radiotherapy		
Yes	7	(17.9%)
No	32	(82.1%)

R-NSM: robotic nipple sparing mastectomy, CPM: contralateral prophylactic mastectomy, NA: not available, SLNB: sentinel lymph node biopsy, ALND: axillary lymph node dissection, LD flap: latissimus drosi flap (harvested at the same time with robotic assisted), ER: estrogen receptor, PR: progesterone receptor, HER-2: human epithelial growth factor receptor type 2.

wound (Fig. 1e).

Breast reconstructions after R-NSM can be performed using prosthetic implant [5,7,9] or autologous tissue with a robotic assisted latissimus dorsi (LD) flap harvest [1,4,19] as patients' need. Implant type breast reconstruction performed in current study was placed in the sub-pectoral muscular pocket [5,10] (Fig. 1f), which was formed by pectoralis major, serratus anterior, and fascia of external oblique muscle, without use of acellular dermal matrix or mesh.

Learning curve evaluation of R-NSM

To evaluate the impact of case experience accumulation to the operation time of R-NSM and immediate prosthesis breast reconstruction (IPBR), the overall operation time, time spent for docking, time for "R-NSM", and specimen weight were gathered and plotted in case sequence (chronological order). The cumulative sum (CUSUM) method was used to analyze the learning curve [18,21]. A learning curve is considered complete when a point for decreasing surgical time was observed from the CUSUM plot.

To objectively evaluate the time spent for R-NSM, each time point was defined and calculated. The "time for docking" was defined from start insertion of single port to completion set-up of da Vinci surgical platform (completion of docking of camera port, monopolar scissor and prograsp forceps). The "time for R-NSM" was defined as after set-up of robotic surgical platform and started skin flap dissection with monopar scissor to the completion of robotic mastectomy and removal of mastectomy specimen. The "time for prosthetic breast reconstruction" was defined after removal of mastectomy specimen to completion of prosthetic implant insertion. The "overall operation time" was defined from start of skin incision to the end of wound closure. The overall operation time also included procedures for axillary surgery, preparation of skin flap, drains placement, and wound closure. Axillary surgeries performed include sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND). Some patients received SLNB, and frozen biopsy revealed metastatic carcinoma then ALND was performed following R-NSM or at the end of breast reconstruction. The "specimen weight" was the weight of the removed mastectomy specimen.

Statistical analyses

Differences in continuous variables were tested by the

Table 2
Peri-operative parameters and complications associated with robotic nipple sparing mastectomy for breast cancer.

All R-NSM (N = 39)							
Blood loss (ml)	37.3 ± 46.5	(10–250)					
Mean mastectomy weight (gm)	266.4 ± 115.0	(45–553)					
Reconstruction implant volume (ml)	326.8 ± 78.8	(130–500)					
Hospital stay (days)	6.7 ± 1.4	(4–9)					
Operation time (mins)	**All R-NSM (N = 39)**		**Group 1 (case 1–13)**		**Group 2 (case 14–39)**		**P value**
Docking time (mins)	10.9 ± 3.9	(6–24)	13.23 ± 4.53		9.77 ± 3.20		0.024
Mean mastectomy time (mins)	100.1 ± 40.7	(56–250)	121.5 ± 58.54		89.38 ± 22.79		0.018
	R-NSM + IPBR (n = 29)		Case 1-12		Case 13-29		
Total RNSM + IPBR time (mins)	257.0 ± 59.7	(169–475)	287.2 ± 77.43		235.6 ± 30.69		0.019
Complication of R-NSM related (N = 39)			**Group 1 (case1-13)**		**Group 2 (case14-39)**		
Delayed axillary wound healing	2	(5.1%)	2	(15.4%)	0	(0%)	
Transient partial nipple ischemia	4	(10.3%)	2	(15.4%)	2	(7.7%)	
Seroma formation needing aspiration	1	(2.6%)	0	(0%)	1	(3.8%)	
Blister formation (small region)	2	(5.1%)	1	(7.7%)	1	(3.8%)	
Skin flap small partial ischemia necrosis[#]	2	(5.1%)	0	(0%)	2	(7.7%)	
Hematoma needing operation	1	(2.6%)	0	(0%)	1	(3.8%)	
Total NAC necrosis	0	(0%)	0	(0%)	0	(0%)	
Implant loss	0	(0%)	0	(0%)	0	(0%)	
Overall complication (N = 39)			**Group 1 (case1-13)**		**Group 2 (case14-39)**		**P value**
Yes	12	(30.8%)	5	(38.5%)	7	(26.9%)	0.486
No	27	(69.2%)	8	(61.5%)	19	(73.1%)	

R-NSM: robotic nipple sparing mastectomy, IPBR: immediate prosthetic breast reconstruction, NAC: nipple areolar complex. [#]management by conservative local wound treatment without surgical excision.

independent *t*-test and are reported as means ± standard deviation (SD). The chi-square test was used for categorical comparisons of data when appropriate. A *p* value of less than 0.05 was considered to indicate statistical significance; all tests were two-tailed. All statistical analyses were performed with the statistical package SPSS (Version 19.0, SPSS, Chicago).

The cumulative sum (CUSUM) method, which is powerful and valuable in the early detection of trends in data [18,21], was used to analyze the learning curve [18]. The method of CUSUM plots [18] used for R-NSM in current study was briefly summarized. Firstly, the mean of all data points was used as a reference value. Then this reference value is subtracted from each data point in succession and any remainder added to the previous sum [18]. Each CUSUM was calculated in chronological order and analyzed the surgical time data by visually inspecting the plots. A learning curve is considered complete when a point for decreasing surgical time was observed from the CUSUM plot [18,21]. All CUSUM analyses were performed with the statistical package "qcc" in R (Version 3.2.2).

Results

During the study period, 39 R-NSMs, which were performed in 33 patients with breast cancer consecutively by the same surgeon at CCH, were identified and comprised the current study. Among these 39 R-NSM procedures, 35 (89.7%) were performed for breast cancer therapeutic consideration and 4 (10.3%) were for risk reducing contralateral prophylactic mastectomy (CPM) (Table 1). Thirty-one (79.5%) of the R-NSM procedures were associated with IBR, and 8 procedures were R-NSM alone. Prosthetic implant insertion was the most frequently (93.5%, 29/31) used breast reconstruction followed by robotic harvested LD flap (6.5%, 2/31) in R-NSM procedures. Axillary lymph node surgery was performed in 84.6% (33/39) of R-NSM procedures. The clinicopathologic characteristics of patients received R-NSM for breast cancer were summarized in Table 1.

The peri-operative parameters associated with R-NSM was summarized in Table 2. The mean blood loss was 37.3 ± 46.5 ml (10–250). The mean operation time for R-NSM, which defined after set-up of robotic surgery platform, was 100.1 ± 40.7 min. The mean operation time for R-NSM and IPBR was 257 ± 59.7 min. The mean hospitalization for R-NSM was 6.7 ± 1.4 days. Data on peri-operative parameters associated with the R-NSM with (or without) IBR are summarized in Table 2.

The time for "docking", "R-NSM", and "total operation for R-NSM and IPBR" were plotted in sequence (Fig. 2). The docking time decreased significantly after cases' experience accumulated. In our first case, it took 24 min for docking. Then after cases' experience accumulated, the time needed for docking could decreased to around 10 min. The time for "R-NSM" and "R-NSM and IPBR" fluctuated between cases, and in mature phase, most of the "R-NSM" and "R-NSM and IPBR" could be completed with 100 min, and 250 min, separately. When mastectomy weight was put into consideration, the time needed to complete R-NSM was highly correlated to the weight of mastectomy specimen (Fig. 2e). It seems that the larger the breast, the longer the operation time was needed in the initial cases. In mature phase, the operation time decreased significantly, and did not fluctuate with specimen weight.

In CUSUM plots analysis of learning curve (Fig. 3), the cases needed to significantly decrease operation time for "docking", "R-NSM", and "R-NSM and IPBR" were 13th, 13th, and 12th procedures, separately. To verify the learning curve derived from CUSUM, patients were separated into different groups (Group 1, initial phase versus Group 2, mature phase) of patients. The "docking time" in initial phase (#1-#13) was 13.23 ± 4.53 min, and 9.77 ± 3.20 min in mature phase (#14-#39, P = 0.024). The "R-NSM time" decreased from 121.5 ± 58.54 min to 89.38 ± 22.79 min (P = 0.018), and total time for R-NSM and IPBR decreased from 287.2 ± 77.43 min to 235.6 ± 30.69 min (P = 0.019, Table 2). Larger mastectomy weight, lymph node metastasis, and phase of learning curve period were factors related to increase operation time for R-NSM or total operation time for R-NSM and IPBR (Table 3). In multivariate analysis (supplementary file), mastectomy weight was the only significant factor (odds ratio 1.203, 95% confidence interval: 0.089–0.280) related to R-NSM or total operation time for R-NSM and IPBR.

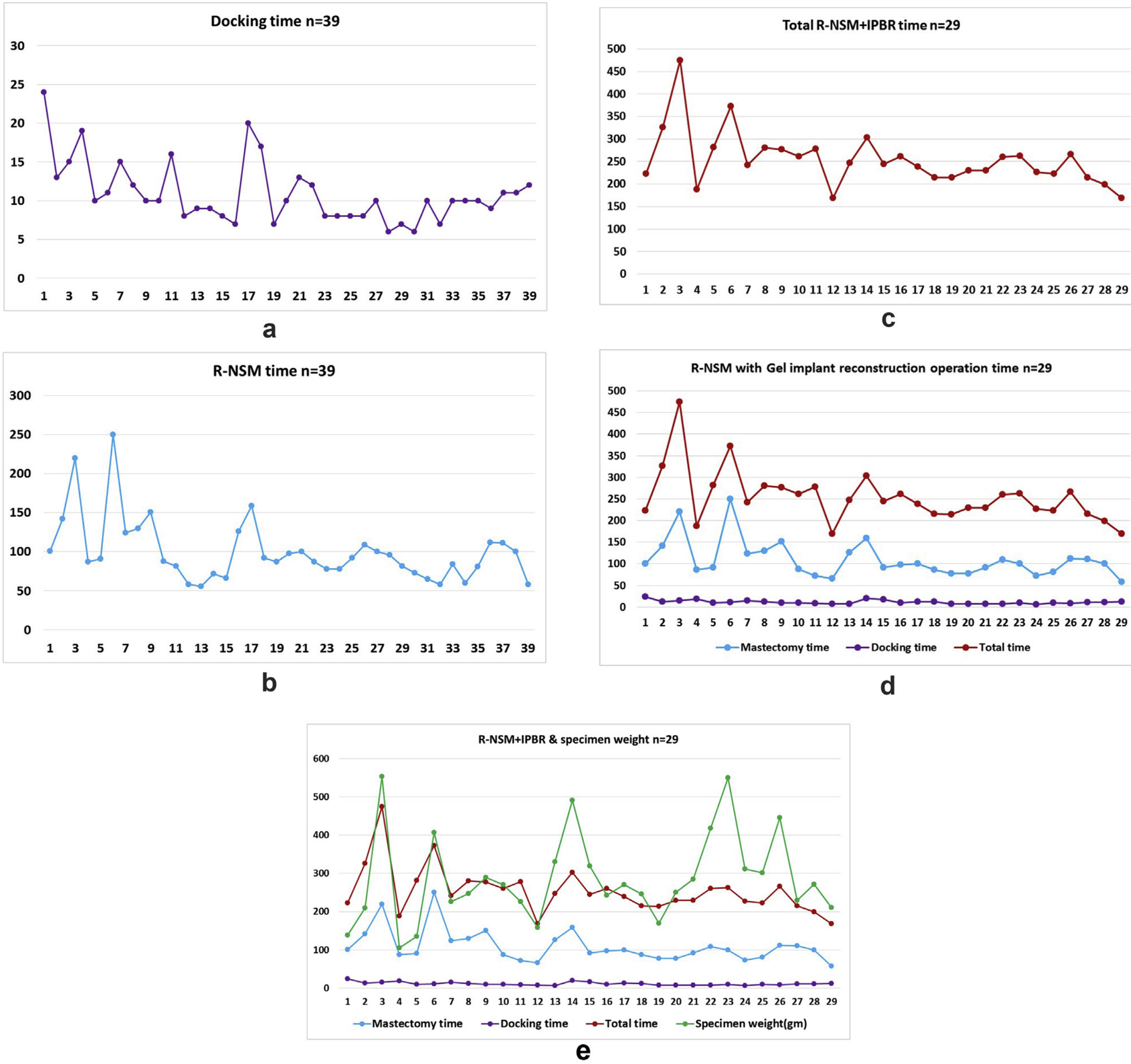

Fig. 2. Operation time and learning curve of robotic nipple sparing mastectomy. (a) The relation between docking time and chronologic cases sequence (n = 39). The docking time decreased significantly after cases' experience accumulated. In our first case, it took 24 min for docking. Then after cases' experience accumulated, the time needed for docking could decreased to around 10 min. (b) Robotic nipple sparing mastectomy (R-NSM time), which was defined as after set up of robotic surgical platform to completion of mastectomy, and chronologic cases sequence (n = 39). The "R-NSM" time was fluctuated between cases, and in mature phase, most of the "R-NSM" could be completed with 100 min. (c) Total R-NSM and IPBR time and chronologic cases sequence (n = 29, 2 procedures were associated with LD flap reconstruction, and 8 procedures were R-NSM alone were excluded). In the R-NSM and IPBR cases, the "total operation time" was also fluctuated between cases. In mature phase, the R-NSM and IPBR usually could be completed within 250 min. (d) Docking time, R-NSM time, total R-NSM and IPBR time versus chronologic cases sequence. (e) Specimen weight correlation with Docking time, R-NSM time, total R-NSM and IPBR time versus chronologic cases sequence.When mastectomy weight was put into consideration, the time needed to complete R-NSM was highly correlated to the weight of mastectomy specimen.

Complication and margin involved rate

In the post-operative morbidity evaluation (Table 2), no implant loss, no major or life-threatening complication was observed. Except one patient, who received bil. R-NSM for right breast cancer and left CPM, suffered from delay bleeding over left breast with hematoma formation needing surgical intervention. The rate of total NAC necrosis for R-NSM was 0%. One (2.9%, 1/35) R-NSM procedure was found to have positive margin involved in the final pathologic check-up. Due to post mastectomy radiotherapy indicated (4 positive nodes) and only small foci of superficial margin involved, this patient received radiation therapy without further surgery. During mean 8.6 ± 4.5 (1.3–16.7) months follow-up, there is no locoregional recurrence, or distant metastasis among these 33 patients.

Discussion

In current study, we reported our preliminary experience of using robotic surgical platform with *da Vinci Si* system to perform 39 NSM in 33 breast cancer patients. Compared with other reported series [7,8], which in some rare occasions (6.9% (2/29) in the Toesca et al.'s report [7], and 1.6% (1/63) in Sarfati et al.'s series [8]) needed to convert to endoscopic or conventional mastectomy, there was no

Table 3
Factors determining time spent for robotic nipple sparing mastectomy (R-NSM) or total operation time for R-NSM and immediate prosthetic breast reconstruction (IPBR).

	R-NSM time (n = 39)				Total R-NSM and IPBR time (n = 29)			
	n	Mean ± SD	range	p	n	Mean ± sd	range	p
Side								
Right	19	113.05 ± 48.64	58–250	0.052	16	272.94 ± 67.38	199–475	0.172
Left	20	87.8 ± 27.42	56–151		13	237.38 ± 43.39	169–326	
Lymph node metastasis								
No	27	90.33 ± 26.81	56–159	0.019	18	235.78 ± 36.03	169–303	0.011
yes	11	124.27 ± 59.48	72–250		10	294.80 ± 78.37	214–475	
Grade								
1	7	117.71 ± 65.79	58–250	0.321	6	261.67 ± 66.67	169–373	0.329
2	16	90.19 ± 25.18	56–142		10	254.90 ± 43.47	169–326	
3	4	99.75 ± 9.84	87–111		4	229.75 ± 22.98	215–263	
Stage								
Tis	10	97.8 ± 32.29	56–159	0.667	7	240.00 ± 29.98	215–303	0.203
I	8	93.63 ± 27.84	58–151		6	239.50 ± 38.45	169–277	
II	12	103 ± 49.74	58–250		10	258.00 ± 54.40	169–373	
III	4	104 ± 29.35	78–142		3	274.00 ± 48.50	230–326	
Lymph node								
No surgery	5	72.2 ± 20.03	56–100	0.142	2	229.50 ± 43.13	199–260	0.066
SLNB	25	100.6 ± 40.01	58–250		19	244.58 ± 46.31	169–373	
SLNB then ALND	7	122.57 ± 49.07	78–220		6	301.33 ± 92.31	230–475	
ALND	1	72 ± NA	72		1	278 ± NA	278	
Specimen weight (gm)								
Small (≤170)	8	77.38 ± 16.12	56–101	<0.001	5	229.60 ± 43.67	169–282	0.026
Medium (<170 - ≤300)	20	94.05 ± 26.85	58–262		14	224.50 ± 39.87	169–326	
Large (>300)	11	127.64 ± 58.62	73–250		10	288.20 ± 78.73	223–475	
Phase of learning curve period								
Group 1[a]	13	121.5 ± 58.54	56–250	0.018	12	287.2 ± 77.43	169–475	0.019
Group 2[b]	26	89.38 ± 22.79	58–159		17	235.6 ± 30.69	169–303	

SD: standard deviation, R-NSM: robotic nipple sparing mastectomy, IPBR: immediate prosthetic breast reconstruction. SLNB: sentinel lymph node biopsy, ALND: axillary lymph node dissection.
[a] For R-NSM time group 1 = case 1-case 13, for total R-NSM and IPBR time group 1 = case 1 - case 12.
[b] For R-NSM time group 2= case 14-case 39, for total R-NSM and IPBR time group 2 = case 13- case 29.

case of robotic procedures had to be converted to standard or endoscopic mastectomy in current report. This might be related to several factors. First, we had accumulated more than 200 endoscopic mastectomy cases experience [11–13,16,17] before we progress to robotic mastectomy [4,5,10,19]. We did not think it is necessary to be master of endoscopic breast surgery to perform robotic breast surgery. But familial with the concept of endoscopic breast surgery would be helpful to proceed to robotic mastectomy. Second, in our initial 2 cases, patients were with small to medium sized breast (Fig. 2e). It would be easier for beginner to perform robotic mastectomy for patient with small to medium sized breast first.

There had been several positions when performing R-NSM either adducted the arm and below the body [6,7] or raising the hand over the head [8,19,22]. The wound incision for R-NSM could be placed over the lateral chest at the level of the NAC or at the bra line for conceal of the wound. As most of our candidates selected for robotic NSM were breast cancer patients, and axillary surgery was usually indicated. We found that by elevating the operative side shoulder to 30° by draping and tilting the table to contralateral side, the arm could be in an abducted position without conflicting the robotic arms. By wound incision placed near the axilla, it would be easier to perform SLNB or ALND, and properly preserve neurovascular bundle in the axilla. In R-NSM, to prevent conflicts with robotic arm and prevent injury, the shoulder and upper arm should be properly placed, and wound incision placement could be adjusted according to preference.

In learning curve analysis, the total operation time was often used as an indicator for the surgeon's experience and ability to complete the operation [16–18]. The shorter or the quick of the operation may reflect that the surgeon was more familial or more competent for the operation. In R-NSM and IPBR procedures, the operation time decreased from 287.2 ± 77.43 min (initial phase, case #1–12) to 235.6 ± 30.69 min (mature phase, case #13–29, P = 0.019, Table 2). The "total operation time" might not be a good indicator for learning curve of R-NSM procedures due to complexity of different axillary operations (SLNB, ALND, or SLNB then ALND) performed, different breast size of patients (45–554 gm, breast Cup A to D), and different difficulties for breast reconstructions (implant size range 130–500 ml) encountered.

Compared with total operation time, "time for R-NSM", which defined as after set up of robotic surgical platform to completion of mastectomy, was a more objective indicator for learning curve of R-NSM (Fig. 2). We observed that 13 cases were needed to decrease the robotic mastectomy time (Figs. 2b and 3b), and time for "R-NSM" decreased from 121.5 ± 58.54 min to 89.38 ± 22.79 min (P = 0.018, Table 2). In contrast to the chronologic case sequence, the R-NSM time was significantly related to specimen weight. In Fig. 2e and Table 3, we could observe that the time needed to complete R-NSM was mainly influenced by weight of mastectomy specimen (odds ratio 1.203). We observed that around 12–13 cases were needed to decrease the robotic mastectomy time, and this was confirmed by the CUSUM plot (Figs. 2 and 3, Tables 2 and 3), and after that R-NSM could usually be completed within 100mins. In our previous study focusing on the learning curve of endoscopic total mastectomy, we observed that around 15–17 cases were needed to decrease the operation time or became more familial with endoscopic total mastectomy [16]. The decreased number of cases for R-NSM compared with E-NSM could be attributed to the more user friendly platform of robotic breast surgery, which contains the 3-dimensional imaging system, flexibility of robotic arm, and instruments.

In Toesca's report [6,7], initially 8.5 to 5 h were needed to complete R-NSM and IPBR, and could be completed within 3 h in

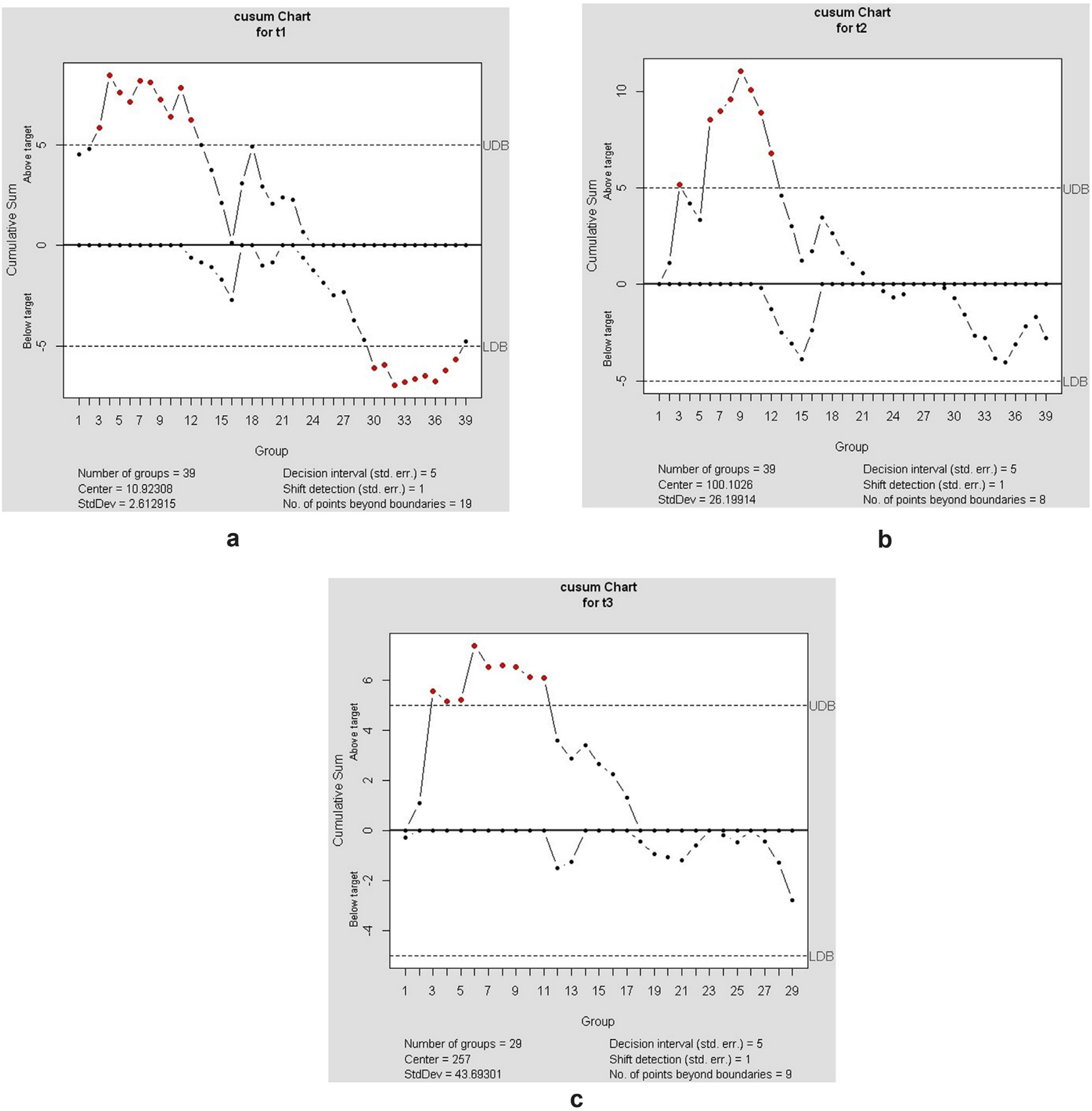

Fig. 3. The cumulative sum (CUSUM) method was used to analyze the learning curve of robotic nipple sparing mastectomy (R-NSM). A learning curve is considered complete when a point for decreasing surgical time was observed from the CUSUM plot. (a) The docking time for 39 patients received R-NSM was tested in CUSM method. The CUSUM curve demonstrated that docking time improved from the 13th case and continued to improve. (b) The "time for R-NSM" of the consecutive 39 R-NSM procedures were tested. The CUSUM curve demonstrated that R-NSM time improved from the 13th case and continued to improve. (c) The "total time for R-NSM and IPBR" of the consecutive 29 R-NSM and IPBR procedures were tested. The CUSUM curve demonstrated that RNSM + IPBR time improved from the 12th case and continued to improve (2 procedures were associated with LD flap reconstruction, and 8 procedures were R-NSM alone were excluded).

mature phase. In Sarfati's report [8], initially it took 200 to 180 min (per breast) to perform R-NSM and IPBR, and in the end of the trial, around 85mins was enough. However, most of these procedures were performed for prophylactic mastectomy (38% (11/29) in Toesca's series, and 98.4% (62/63) in Sarfati's), which axillary lymph node surgery and sub-nipple biopsy were not needed, and in small to medium sized breast (78–330 gm, breast cup A to C) [7,8]. Furthermore, the breast reconstruction in Sarfati's series were performed in a pre-pectoral manner [8,9], which omitted the dissection of sub-muscular plane. In contrast, 89.7% (35/39) of R-NSM in current series were therapeutic for breast cancer. The longer operation time in current study also reflected more complexity (axillary lymph node surgery, sub-nipple frozen biopsy, and dissection of subpectoral muscular pocket) of the surgery need to be performed in this cohort of patients.

This is the first study as we know focusing on the learning curve of R-NSM. CUSUM plots, and factors affecting the operation time were also discussed. We revealed that time for R-NSM fluctuated with mastectomy weight, and this fluctuation could be reduced after cases experience accumulated. From our preliminary experience, R-NSM and IPBR (or R-NSM alone) is a safe procedure, and could be a promising new technique for breast cancer patients indicated for mastectomy. Current study provides some valuable information for the development and patient selection for robotic surgery in total skin and nipple preserving type mastectomy.

Author disclosures

None of the authors have conflicts of interest or financial ties to disclose.

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Conflict of interests statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2018.09.021.

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