Analysis of the Movement of Surgical Clips Implanted in Tumor Bed during Normal Breathing for Breast Cancer Patients

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Purpose: To evaluate the movement of surgical clips implanted in breast tumor bed during normal breathing. Materials and Methods: Seven patients receiving breast post-operative radiotherapy were selected for this study. Each patient was simulated in a common treatment position. Fluoroscopic images were recorded every 0.033 s, 30 frames per 1 second, for 10 seconds in anterior to posterior (AP), lateral, and tangential direction except one patient's images which were recorded as a rate of 15 frames per second. The movement of surgical clips was recorded and measured, thereby calculated maximal displacement of each clip in AP, lateral, tangential, and superior to inferior (SI) direction. For the comparison, we also measured the movement of diaphragm in SI direction.

Results: From AP direction's images, average movement of surgical clips in lateral and SI direction was 0.8 ± 0.5 mm and 0.9 ± 0.2 mm and maximal movement was 1.9 mm and 1.2 mm. Surgical clips in lateral direction's images were averagely moved 1.3 ± 0.7 mm and 1.3 ± 0.5 mm in AP and SI direction with 2.6 mm and 2.6 mm maximal movement in each direction. In tangential direction's images, average movement of surgical clips and maximal movement was 1.2 ± 0.5 mm and 2.4 mm in tangential direction and 0.9 ± 0.4 mm and 1.7 mm in SI direction. Diaphragm was averagely moved 14.0 ± 2.4 mm and 18.8 mm maximally in SI direction.

Conclusion: The movement of clips caused by breathing was not as significant as the movement of diaphragm. And all surgical clip movements were within 3 mm in all directions. These results suggest that for breast radiotherapy, it may not necessary to use breath-holding technique or devices to control breath.

Key Words: Breast cancer, Radiotherapy, Surgical clips

Introduction

A prerequisite for conformal radiotherapy and intensity-modulated radiotherapy is the accurate localization of target volume.^{1,2)} Therefore, it is important to quantify the uncertainties caused by organ motions and daily set-up errors. In ICRU Report 50,³⁾ a planning target volume (PTV) was defined as a

geometrical concept to account for the set-up errors and internal organ motions and it includes the clinical target volume (CTV), accepting the uncertainty in its definition. Although the reduction of the PTV margin is generally desirable in radiotherapy, it must be accompanied by the assurance that the risk of geometric misses does not increase.⁴⁾

The uncertainty in position of organs during radiotherapy is one of the major problems in achieving high treatment outcome. Motion of tumors due to breathing is present in the lung, breast, liver, kidney and other disease sites.⁵⁾ Many researchers have addressed the movement of various organs such as diaphragm,⁶⁾ lung,¹⁾ liver,⁷⁾ and prostate⁸⁾caused by breathing. Based on these studies, expansion of treatment volume is required for ensuring appropriate coverage of target.

In breast radiotherapy with tangential method, the attempt for

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Submitted July 20, 2006, accepted August 18, 2006

This work was supported by the Korea Research Foundation Grant funded by the Korean Government (MOEHRD) (R04-2002-000-20143-0).

reducing target volumes have been developed to decrease irradiation to normal tissue such as heart, lung, and liver. Active breathing control (ABC),⁴⁾ aperture maneuver with compelled breath (AMC),⁹⁾ and deep-inspiration breath-hold (DIBH) technique ^{10~13)} have been used to reduce the movement of target, thereby decreasing normal tissue complication. One of the disadvantages for applying these techniques to patient treatment is the increased treatment time.^{4,9)} In addition, some patients such as pulmonarily compromised patients could not tolerate these methods.⁵⁾

In many studies, measuring chest wall movement due to breathing was the method for evaluating the movement of breast. ^{10,13,14,24)} However, chest wall was not involved in breast tumor bed, measuring the chest wall may not indicate the breast motion. In this study, we analyzed the motion of breast during normal breathing using surgical clips implanted in the breast tumor bed. Surgical clips in breast lumpectomy cavity have been used as a reference for determining tangential and electron boost irradiation in many researches. ^{15,18–20)} Weed et al ¹⁵⁾ and Baglan et al ¹⁶⁾ already reported the treatment margin based on the surgical clip movement using CT scan in free breathing, normal inspiration, and normal expiration. However, no study has been performed for measuring the real breast motion. For determining a treatment margin, accurate measurement of breast motion is needed.

The purpose of this study is to evaluate the movement of surgical clips implanted in breast tumor bed during normal breathing. We detected and analyzed the movement of the clips compared with that of diaphragm utilizing fluoroscopic images.

Materials and Methods

Seven patients receiving breast post-operative radiotherapy after breast conserving surgery from September to November 2003 were selected for this study. Each patient's information is shown in Table 1. Kovner et al¹⁸⁾ reported that for marking the length, width, and depth of the tumor bed, at least five clips should be inserted optimally. In our institution, physicians inserted five to seven surgical clips in the breast cavity at the time of surgery to identify the margins of the tumor bed (medial, lateral, superior, inferior, at the center and at the deepest portion of the tumor bed from the external excision). ¹⁸⁾

Each patient was simulated in a common treatment position. Patients were positioned on a table with both arms elevated. Image recording was synchronized with a common simulation process. Patients didn't have any restriction of breathing during the simulation. Fluoroscopic images were recorded in anterior to posterior (AP), lateral, and tangential direction for 10 seconds in each direction (Fig. 1). The images were recorded in 30 frames per second, i.e. 0.033 s per one frame, except one image (Patient number 5) which was recorded as a rate of 15 frames per second.

The movement of the surgical clips was traced by a commercial software (Adobe[®] After Effects[®] Professional Ver. 6.5) to calculate the offset of the position of the clips as a function of time (Fig. 2). For each image, surgical clips were identified from the first frame. When determining a track point, we appointed it at the end of a clip. Track motion was made

Table 1. Summary of Properties of Each Patient and Number of Clips Identified in Simulation Film and Fluoroscopic Images in First Frame of Each Image

					Number	of clips	
Patient no.	Position of irradiated breast	Stage	Age	Circulation	F	uoroscopic im	age
				Simulation —	AP [†]	Lateral	Tangential
1	Right UOQ*	IIIA	65	6	3	3	4
2	Right UIQ [†]	IIA	38	6	3	5	5
3	Right UOQ	IA	50	7	1	3	3
4	Right UIQ	0	34	5	4	2	4
5	Left UOQ	I	36	5	1	3	4
6	Right UIQ	IIA	47	6	6	3	5
7	Left UIQ	IIB	48	6	4	3	5

^{*}upper outer quadrant, †upper inner quadrant, †anterior to posterior

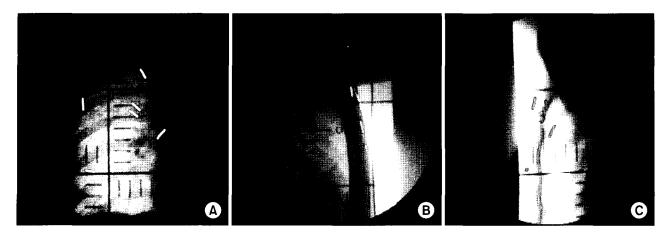
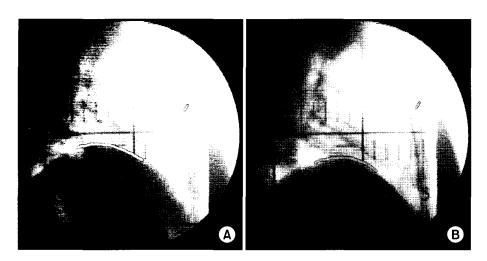


Fig. 1. Fluoroscopic images of a patient in (A) AP, (B) lateral, and (C) tangential directions at time.



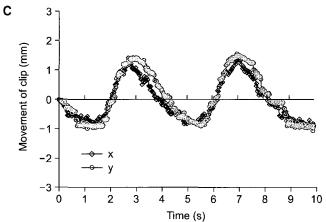


Fig. 2. The comparison of position of clip and diaphragm in (A) 0 and (B) 2 seconds. (C) Movement of the same clip as a function of time.

by following the point which had same brightness of the track point in the first frame. The end of the clip had most contrast compared with a soft tissue in human body, thereby made a point at the end of the clip. Data recording the movement of each surgical clip as a function of time was in the timeline window. These data were copied and collected using Microsoft[®] Excel[®] software. The position of surgical clips in each frame were recorded as pixel values. It was needed to convert pixel values to millimeter values. The pixel values were divided by 2.5 because 1 cm in the fluoroscopic images contains 25 pixels.

The movement of the clips was plotted by considering first frame's x and y direction's tracking point values as a starting point. In some cases, it was not possible to track the clip movement automatically due to charge in contrast for one frame to another. In these cases, clips were traced manually and modified the tracking value deviating from the real clip position. The movement of all the clips was measured and recorded by above method. By this measurement, we calculated upper and lower movement of each surgical clip, and maximal amplitude of surgical clip movement in three directions.

For analyzing the effect of breathing motion to breast movement, we divided the surgical clips which were located above or under the isocenter based on SI direction and compared the movement of these clips. As surgical clips under the isocenter were more located near the diaphragm, we compared the divided surgical clip movement.

For comparing the movement of surgical clips, we measured the movement of diaphragm in fluoroscopic images in SI direction. For 10 seconds, the maximal and minimal position of diaphragm was contoured in each fluoroscopic image by a physician (J. Lee, M.D.) using the commercial software (Fig. 3). We placed a point to each diaphragm's apex in the images which diaphragm was located maximally and minimally and calculated the maximal amplitude of the diaphragm movement in SI direction. For a patient (Patient number 6), as movement of diaphragm was beyond the image field, so it was impossible to detect the movement of diaphragm in lateral and tangential

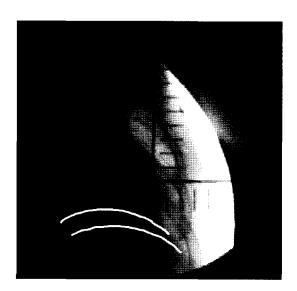


Fig. 3. An example of maximal and minimal diaphragm position from a patient.

direction's images. We compared the movement of surgical clips and diaphragm for analyzing the effect of breathing motion to the surgical clip movement.

Results

Surgical clips detected in fluoroscopic images in each direction are shown in Table 1. Total number of the surgical clips in the images are 22 (AP), 22 (Lateral), and 30 (Tangential). As seeing in the table, the clips were less visible in the fluoroscopic images than in the simulation films. It was caused by overlap of some clips or clips' cover-up by the movement of other organs. When a clip was located near the bone, heart, or diaphragm, it was difficult to detect the clip's position.

In AP direction's fluoroscopic images, average movement of all the detected surgical clips in x (lateral) and y (SI) direction was 0.8 ± 0.5 mm and 0.9 ± 0.2 mm and maximal movement was 1.9 mm and 1.2 mm, respectively. In lateral direction's images, average and maximal movement of the 22 surgical clips was 1.3 ± 0.7 mm and 2.6 mm in x (AP) direction and 1.3 ± 0.5 mm and 2.6 mm in y (SI) direction. Average movement of surgical clips detected in tangential direction's fluoroscopic images was 1.2 ± 0.5 mm in x (tangential) direction and $0.9\pm$ 0.4 mm in y (SI) direction and maximal movement in tangential and SI direction was 2.4 mm and 1.7 mm, respectively (Table 2). Average and maximal movement in SI direction is larger in lateral direction than in AP or tangential directions. This is because surgical clips detected in three direction's images were not the same due to invisible clips in the fluoroscopic images. Maximal movement in SI direction of each clips didn't show larger movement in certain direction's image (Data not shown).

Table 2. Maximal and Average Amplitude of Maximum Movement of Surgical Clips in All Seven Patients Obtained from AP (Anterior-Posterior), Lateral, and Tangential Directions

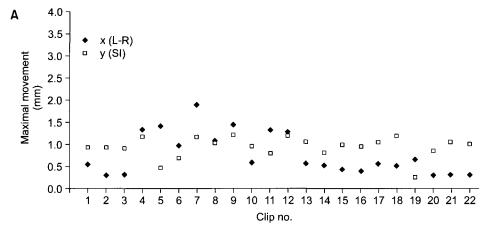
	AP (m	ım) [†]	Lateral	(mm)	Tangential	(mm)
	Lateral	SI §	AP	SI	Tangential	SI
Max* Ave [†]	1.9 0.8	1.2	2.6 1.3	2.6 1.3	2.4 1.2	1.7 0.9

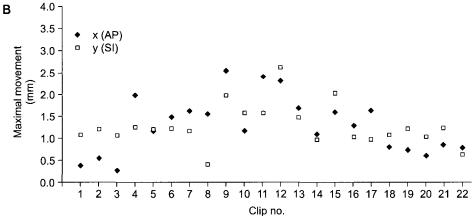
*maximum amplitude, [†]average amplitude, [†]anterior to posterior direction, [§]superior to inferior direction

Maximal movements of each surgical clip measured in AP, lateral, and tangential direction's images are shown in Fig. 4.

Table 3 shows average movement of clips of each patient. The largest movement of clip observed in patient 3 is 1.89 mm/1.16 mm, 2.04 mm/1.71 mm, and 2.01 mm/1.32 mm in x/y direction in AP, lateral, tangential images, respectively. In lateral images, patient 4 had the largest movement 2.04 mm in SI direction.

Surgical clips located under the isocenter in y direction were 6/22 (27%), 4/22 (18%), and 6/30 (20%) in AP, lateral, and tangential direction's images, respectively. And four out of the seven patients showed the position of the surgical clips above the isocenter. Average movement of surgical clips located above the isocenter in x/y direction was 0.8 ± 0.5 mm/ 1.0 ± 0.2 mm, 1.3 ± 0.7 mm/ 1.3 ± 0.5 mm, 1.2 ± 0.5 mm/ 1.0 ± 0.4 mm in AP, lateral, tangential direction's images, respectively. Surgical clips





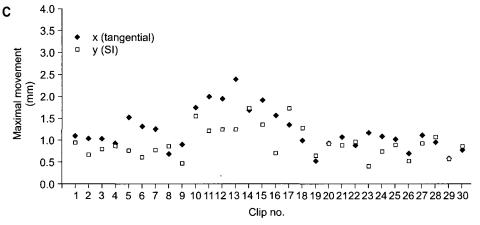


Fig. 4. Frequency plot of the variation of the clip position in (A) AP, (B) lateral, and (C) tangential directions.

Table 3. Average Amplitude of Maximum Movement of Surgical Clips of Each Patient Obtained from AP (Anterior-Posterior), Lateral, and Tangential Directions

		A	Average n	novemer	ıt			
Patient no.	AP*		Lateral		Tanger	ntial		
	Lateral	SI [†]	AP	SI	Tangential	SI		
1	0.37	0.91	0.40	1.12	1.01	0.80		
2	1.23	0.77	1.57	1.05	1.13	0.68		
3	1.89	1.16	2.04	1.71	2.01	1.32		
4	1.11	0.93	2.00	2.04	1.88	1.25		
5	1.28	1.18	1.32	1.34	0.95	1.14		
6	0.50	1.01	1.06	1.09	1.03	0.77		
7	0.39	0.78	0.76	0.97	0.81	0.78		

^{*}anterior to posterior, †superior to inferior

located under the isocenter were averagely moved 0.8 ± 0.5 mm/ 0.8 ± 0.2 mm, 1.2 ± 0.6 mm/ 1.2 ± 0.2 mm, 1.3 ± 0.3 mm/ 0.9 ± 0.3 mm in x/y directions in AP, lateral, tangential images, respectively. The difference between the mean movement of surgical clips was within 0.2 mm. Therefore, we knew that the movement of surgical clips was not influenced by the breathing motion.

Movement of surgical clips in lateral direction was averagely less than in AP, SI, and tangential direction. However, as difference between average movements in three directions was within 0.5 mm, the difference was not significant. For including tumor bed considering breathing motion, 3 mm treatment margin was enough to cover surgical clip movement for all the patients. 2 mm margin included 86% (19/22) of AP direction's clip movement, 100% (22/22) of lateral direction's clip movement, and 97% (29/30) of tangential direction's clip movement. In SI direction, 2 mm margin included 100% (22/22), 91% (20/22), 100% (30/30) of surgical clip movement in AP, lateral, tangential direction's images, respectively.

The movement of diaphragm, on the other hand, was significantly larger than that of the surgical clips. In SI direction, the diaphragm was moved averagely 14.0 ± 2.4 mm with the maximum movement 18.8 mm. Compared with the motion of the diaphragm, the movement of surgical clips in the breast tumor bed was considerably small. Therefore, movement of surgical clips implanted in the breast tumor bed was not correlated with the movement of diaphragm. A result of measuring the movement of diaphragm in each direction's image are shown in Table 4.

Table 4. Maximal Movement of Diaphragm in SI Direction during Normal Breathing for Each Patient

D .:	Movement (mm)				
Patient no.	AP	Lateral	SI		
1	11.2	14.0	16.1		
2	11.9	12.6	8.6		
3	14.9	12.4	15.2		
4	16.4	14.3	16.0		
5	18.8	12.0	15.2		
6	16.2				
7	14.8	13.6	11.6		
Average		14.0			

Discussion

The main goal of radiation therapy is delivering dose to target volume, while sparing normal tissue. There are sensitive organs near breast such as liver, lung, and heart, etc. and reducing dose delivered to these organs is a major concern of breast radiotherapy planning. And the purpose of radiation therapy of breast cancer patients is the reduction of local recurrence rate. ¹⁷⁾ Implanting surgical clips in breast excision cavity was done in many institutions and it was used as the reference of determining radiation field, especially electron boost field. ^{17~21)} In our institution, supplemental boost of 10.0 Gy was followed after whole breast irradiation based on the position of surgical clips.

In this study, we attempted to evaluate the internal motion of surgical clips in the breast excision cavity. The movement of surgical clips was within 3 mm in all three directions and the movement was significantly smaller than that of diaphragm. From Ford et al. 6 diaphragm was averagely moved 6.9 ± 2.1 mm without gating and 2.6 ± 1.7 mm with gating. Compared with the result by this study and Ford et al, 6 surgical clip movement was not correlated with the breathing motion. And the movement of surgical clips showed better immobilization of breast tumor bed than using deep-breath hold technique or immobilization devices. Pedersen et al. 17) evaluated the feasibility of a breath-hold technique for breast cancer and showed that the mean anterioposterior chest wall excursions were 2.5, 2.6, and 4.1 mm during free breathing, expiration breath-hold, and deep-inspiration breath-hold, respectively. The results in this study showed that surgical clip movement was not significantly influenced by breathing motion. It is agreed well with a previous study that reporting the insensitivity of breathing motion to whole breast radiotherapy by Frazier et al.²²⁾

Our evaluation of surgical clip movement gives information of treatment margin for breast cancer patients during normal breathing. As surgical clips represent the breast tumor bed borders, measurement of the movement of the clips will provide the information for determining treatment margin.

Treatment margin is needed to cover treatment target volume including set-up error and organ motion. Margin used to define the planning target volume (PTV) is 1 cm. Hurkmans et al²⁾ said that PTV was constructed by expanding the clinical target volume (CTV) by 7 mm. Hanley et al $^{12)}$ also showed that $1\!\sim\!2$ cm margin is needed for free-breathing plans and $2\sim5$ mm for deep-inspiration breathing-hold plans. Based on the results, we concluded that 3 mm treatment margins are sufficient for breast cancer radiotherapy including breast tumor bed motion during normal breathing if set-up error is minimized. These treatment margins are much less than the 5 mm ITV (irradiated tumor volume) margins suggested by Weed et al 15 and Baglan et al 16 measuring the movement of surgical clips using CT scans. And the 3 mm margins are the same as previous studies using respiratory control techniques. Suh et al⁹⁾ reported that additive margins needed for a moving target with aperture maneuver with compelled breath (AMC) are not larger than 3 mm for the respiratory organ motion. Remouchamps et al²³⁾ also suggested 3 mm margins in the mid- thorax region with moderate deep inspiration breath hold (mDIBH). Surgical clips were moved maximally 2.6 mm in AP and SI direction and maximal lateral direction was less than in AP and SI direction. We know that it may not necessary to use breath holding device to reduce PTV since the movement of clips is not as large as respiratory motion.

Based on this study, we know that breast tumor bed was not significantly moved by breathing motion compared with diaphragm during normal breathing, however, sample size of our study is small, it is needed to be confirmed through further study. The treatment margins suggested in this study were valid during normal breathing condition. If patients breathe deeply during radiotherapy, surgical clip movement can be much larger than during normal breathing. So, the treatment margin based on the surgical clip movement during normal breathing may not cover the breast tumor bed motion. Therefore, for defining

treatment margins covering the breast motion due to deep breath, we will measure the movement of surgical clips in deep breath in following study.

Analyzing the movement of breast tumor bed is one of the important factors for breast radiotherapy. Many researches addressed the respiratory gating technique for immobilizing treatment target, thereby achieving high treatment outcome. However, from the surgical clip movement, breast tumor bed movement could be sufficiently included by 3 mm margins without using breathing control device or technique. Based on this study, it can be concluded that breast tumor bed was not moved significantly than respiratory motion. Therefore, the movement of the breast tumor bed was not considerable for using immobilization devices or technique.

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--- 국문초록 ---

유방암 환자의 정상 호흡에서 종양에 삽입된 외과적 클립의 움직임 분석

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목 적: 정상 호흡에서 외과적 클립을 이용하여 유방 종양의 움직임을 평가하였다.

대상 및 방법: 유방 보존 수술 후 방사선 치료를 받은 7명의 환자를 대상으로 하여 각 환자별로 일반적인 모의 치료 과정에서 형광 투시 영상을 얻었다. 한 환자의 영상만 매초 15프레임의 비율로 기록되었고, 다른 환자들의 영상은 1초당 30프레임의 비율로 앞뒤, 옆, 빗나가는 방향에서 기록되었다. 각 클립의 원점에서의 최대, 최소 움직임을 측정하였고 이를 통하여 클립마다 각 방향에서의 최대 움직임을 계산하였다. 비교를 위하여 위-아래 방향으로의 횡경막의 움직임도 측정하였다.

결과: 앞뒤 방향의 영상으로부터 옆 방향과 위-아래 방향으로의 외과적 클립의 평균 움직임은 0.8 ± 0.5 mm, 0.9 ± 0.2 mm이며, 최대 움직임은 1.9 mm, 1.2 mm였다. 또한, 옆 방향 영상에 나타난 클립들은 평균적으로 앞-뒤 방향으로 1.3 ± 0.7 mm, 위-아래 방향으로 1.3 ± 0.6 mm 움직였으며, 최대 움직임은 각각 2.6 mm, 2.6 mm였다. 빗나가는 방향의 영상에 있는 외과적 클립들의 평균 움직임과 최대 움직임은 비스듬한 방향에서는 1.2 ± 0.5 mm와 2.4 mm였으며, 위-아래 방향으로는 0.9 ± 0.4 mm와 1.7 mm였다. 횡격막은 위-아래 방향으로 평균적으로 14.0 ± 2.4 mm 움직였으며, 최대 18.8 mm 움직였다.

<u>결</u>론: 호흡에 의해 발생되는 클립의 움직임은 횡경막의 움직임에 비해서 크지 않은 것으로 나타났다. 그리고, 외과적 클립의 움직임은 모든 방향에서 3 mm 이내였다. 이 결과, 유방암의 방사선 치료 시 호흡을 잡아주는 기술이나 도구가 필요하지 않다는 것을 알 수 있었다.

핵심용어: 초기 유방암, 방사선 치료, 외과적 클립