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Effect of Breathing on Contralateral Breast Doses in Patients with Breast Carcinoma Receiving Radiotherapy

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ABSTRACT

Objectives: Radiotherapy (RT) for breast cancer results in scattered radiation doses to the contralateral breast (CB) which is found to be associated with an increased risk of secondary malignancy. This study investigates the dosimetric and volumetric changes in CB as a consequence of changes during the breathing cycle.

Patients- Methods: Ten patients with breast carcinoma underwent breast conservative surgery or mastectomy receiving RT are included. For this study, planning CT (computerized tomography) images were obtained during deep inspiration (I) and end of expiration (E), as well as free breathing (FB) in order to simulate respiratory cycle. I and E images were registered to FB. Targets and CB were contoured by the same Radiation Oncologist on 3 image series. Three dimensional conformal or IMRT planning was done to obtain dose - volume information. Treatment plans and dose calculations were constructed using CT images taken during FB. Then, plan was exported to I and E image series. The significance of dose and volume changes was investigated.

Results: Mean breast doses changed marginally between FB and I (p=0,057) while not significant between FB and E (p=0.58). There was a significant variation between I and F, and I and E for 1% of CB volume receiving maximum dose (p=0.008 and p=0.03) while it was not significant between FB and E (p=0.35). Intended dose constrains for CB were achieved for all patients as mean CB doses were less than 1 Gy and max CB doses were less than 3.5 Gy. However, these limitations exceeded during I phase in 6 out of 10 patients regarding maximum CB doses and 1 out of 10 patients for mean CB dose.

Conclusion: Contralateral breast dose changes should be considered together with heart and lung dose changes during the different phases of respiratory cycle because maximum CB dose could exceed the upper limit in 60% of patients during I.

Kew words: breast carcinoma, radiotherapy, contralateral breast dose, breathing

RADYOTERAPİ UYGULANAN MEME KANSERLİ HASTALARDA SOLUNUM HAREKETLERİNİN KARŞI MEME DOZUNA ETKİSİ

ÖZET

Amaç: Radyoterapi (RT) sırasında karşı memeye (CB) saçılan ışınların artmış ikincil kanser gelişmesiyle ilişkisi bulunmuştur. Bu çalışmada solunum siklusu boyunca karşı meme hacmi ve dozunun değişimi incelenmiştir.

Hastalar ve Yöntemler: Meme kanseri tanısıyla meme koruyucu cerrahi veya mastektomi uygulanmış 10 hasta çalışmaya alındı. Bu çalışmaya özel olarak, planlama amacıyla kontrolsuz solunum (FB) yanında, derin inspirasyon (I) ve ekspirasyon sonu (E) bilgisayarlı tomografi görüntüleri de alındı. I ve E imajları FB imajlarına çakıştırıldı. Target ve CB hacimleri aynı Radyasyon Onkoloğu tarafından 3 seride de belirlendi. Doz- hacim verilerini elde etmek amacıyla 3 boyutlu konformal veya yoğunluk ayarlı radyoterapi teknikleri ile FB serisi kullanılarak planlama yapıldı. Daha sonra plan I ve E serilerine aktarıldı. Doz ve hacimde oluşan farklılıklar değerlendirildi.

Bulgular: Ortalama CB dozu F ve E arasında anlamlı farklılık göstermemesine (p=0.58) karşın F ve I arasında sınırda anlamlı (p=0.057) farklılık gösterdi. En yüksek dozu alan %1'lik hacim değeri I ile FB ve I ile E arasında anlamlı olarak (p=0.008 ve p=0.03) değişirken FB ile E (p=0.35) arasında anlamlı fark gözlenmedi. FB imajları kullanılarak yapılan planlamada CB için öngörülen kısıtlamalar olan; ortalama CB dozunun 1Gy'den az olması ve en yüksek CB dozunun 3,5 Gy'den az olması tüm planlarda sağlandı. Ancak I sırasında 10 hastanın 6'sında maksimum CB dozu ve 1'inde ortalama CB dozu öngörülen sınırları aştı.

Sonuç: Hastaların %60'ında ortalama CB dozu belirlenen limitleri aşabileceğinden, kalp ve akciğer dozlarının yanında CB dozunun da solunum hareketleriyle değişimi izlenmelidir.

Anahtar sözcükler: meme kanseri, radyoterapi, karşı meme dozu, solunum

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Introduction

Life expectancy has been increasing for breast carcinoma patients as a result of screening programs providing early stage diagnosis and treatment approaches like new chemotherapeutics, targeted agents and advanced radiotherapy (RT) technology (1). Treatment related morbidity and secondary cancers have become an important issue for this group of patients. Therefore, it is important to reduce exposed organ at risk doses such as heart, lung and contralateral breast (CB) (2, 3, 4, 5). Contralateral breast carcinoma is the most common secondary malignancy in breast carcinoma patients with an incidence of 1.2- 12% (6, 7, 8, 9). This rate is affected by patient's age, disease stage, histological type, genetic background, follow-up time, treatment type such as chemotherapy, hormonal therapy and RT (6, 10, 11). Radiation therapy is found to be associated with an increased risk of CB carcinoma (6, 8,12, 13, 14,15) and risk ratio is slightly increased with scattered radiation dose to the CB especially in patients younger than 45 years-old (6,16). Therefore, scattered radiation dose is important, needs to be considered seriously and should be reduced as much as possible. Respiratory gated radiation therapy gained wide attention because it could provide reduced cardiac and lung doses (3, 4, 17). However, CB dose changes during respiration cycle should be examined. This prospective study investigates the dosimetric and volumetric changes in CB as a consequence of breathing cycle.

Methods and Materials

Ten patients with left breast carcinoma underwent breast conservative surgery (BCS) or mastectomy (M), receiving RT (breast, chest wall, and regional lymph nodes) were included. Studies searching target and organs at risk namely heart, lung and CB dose changes with breath cycle were initiated in 2009 in our clinic and part of the results were published elsewhere.

All patients were given oral explanation regarding the maintenance of breath hold during inspirium and end of expirium by the treating physician. Additionally, they were physically trained by a dedicated therapist and an adequate understanding of the procedure was ensured. All patients were positioned supine on carbon fiber breast board having fixed base with adjustable tilting to ensure the sternum horizontal position with ipsilateral arm above the head, and a body cast fabricated to immobilize patient's shoulder was used to ensure daily set-up accuracy. All patients were scanned with a multi-detector 16 slice CT (Siemens sensation 16 Erlangen, Germany), in the treatment position on a flat table top.

Images were obtained as three different sets of series which were taken without breath control (F), deep inspiration (I), and end of expiration (E), with 3-mm interval. As such, whole breath cycle was simulated. Images were transferred as DICOM III format via network between CT and treatment planning system (TPS). ECLIPSE version 8.6 (Varian Palo Alto USA) RT planning system was used for planning. For this study, CT images taken during I and E were registered to FB, according to DICOM coordinates (Figure1) Target (breast) and organ at risk (OAR) [lung, heart, LAD (left anterior descending artery), CB] were delineated on three series. Our in-house protocol require that CB volume receiving 3.5Gy must be less than 1% and mean CB dose should be less than 1 Gy. For each patient, the initial treatment plans were constructed on F series using three dimensional conformal techniques. Beam data were transferred from FB to I and E image series. All radiation plan properties such as beam angles, wedges, field size, MU etc were kept the same. Because of target and OAR displacement secondary to breathe cycle, transferred beams were not optimal for I and E breath cycles. Nonetheless, plan optimization or any alterations were not made. Dose calculation was done using only considering the heterogeneity correction. By this means, target and OAR dose distributions for E and I image series were obtained.

This particular part of the study examined exposed dose and volume variations of CB during breath cycle. In an effort to analyse this, 1% volume receiving maximum dose and mean CB dose, 1 Gy exposured CB volume (V1Gy), maximum 2cc CB dose (D 2cc) for FB, I and E series were examined as endpoints. The significance of dose and volume changes were investigated using non-parametric *t*-test (Wilcoxon).

Result

For whole group, average CB volume for FB, I and E did not significantly change with breath cycle (p=0,392). Detailed dose - volume information as mean, maximum and 1% CB volume receiving max dose, volume receiving $\geq$ 1Gy, 2ml volume receiving doses according to each breast cycle for whole group are shown at Table 1. Mean CB doses changed marginally significant between FB and I series (p=0,057) while the change was not significant between FB and E (p=0.58) (Figure 2a). There was a significant variation between I and FB, and I and E for 1% volume receiving

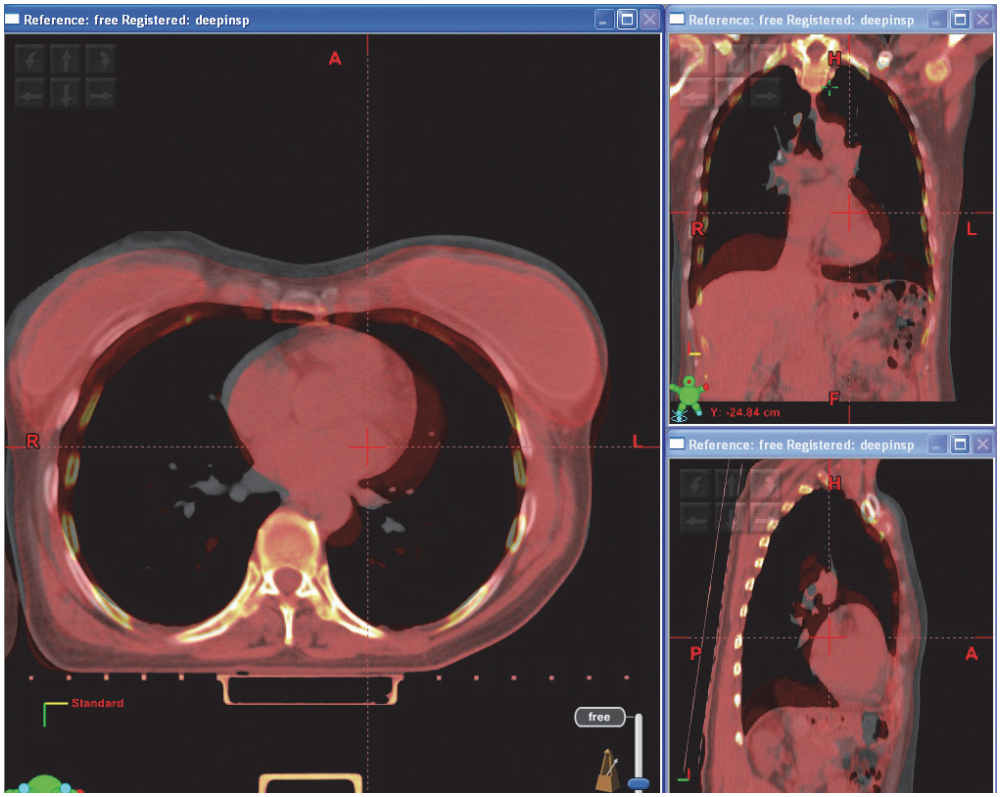


Figure 1. Target and organs at risk changes according to breath cycle

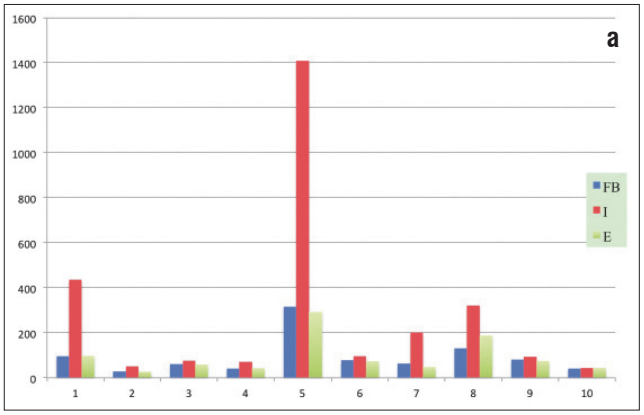
maximum dose (p=0.008 and p=0.03) while it was not significant between FB and E (p=0.35) (Figure 2b). Significant variation was seen for 2ml volume receiving doses for different phases of respiration (Figure 3). As seen on the figures intended dose constrains for CB were achieved for all patients as mean CB doses were less than 1Gy and max CB doses were less than 3.5Gy for all patients. However, these limitations were exceeded during I phase for 6 out of 10 patients regarding maximum CB doses and 1out of 10 patients for mean CB dose (Figure 2a and 2b).

Discussion

There were no significant differences in breast volume contoured in different phases of breath cycle as expected. It was claimed that RT related secondary malignancies increase with radiation exposed volume and dose (16, 18, 19). Therefore, Radiation Therapy Oncology Group recommends limiting CB dose and exposed volume (20); theoretically, these limitations would be helpful to prevent secondary malignancies. For this reason we have

Table.

Patient No	*CB volume >1 Gy (cc) (FB)*	*CB volume >1 Gy (cc) (I)*	*CB volume >1 Gy (cc) (E)*	*2cc CB dose (cGy) (FB)*	*2cc CB dose (cGy) (I)*	*2cc CB dose (cGy) (E)*
1	159	348	161	366	5190	381
2	14	126	17	127	272	137
3	60	120	57	174	231	168
4	80	103	78	246	258	230
5	113	99	104	1458	3179	1381
6	113	104	148	405	401	490
7	56	53	28	249	522	180
8	445	650	650	853	5709	4264
9	74	112	60	208	306	191
10	59	74	72	284	295	294



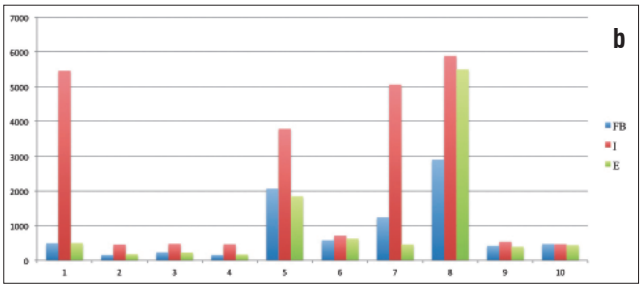


Figure 2. **a.** Mean breast doses for each patient according to different phases of the breath cycle.
b. Max breast doses for each patient according to different phases of the breath cycle

an in-house dose restriction protocol. However, as the results of this study demonstrated, there was a tendency of increase in CB dose in I when compared to E and F. Even though, RT planning provided intended CB doses using images taken during FB, in practice respiratory cycle could change the actual exposed dose and violate the plan. Therefore, breathing cycle needs to be considered in treatment planning and limited doses should be provided not only for FB, but also for I and E phases. Consequently, images taken during inspirium should be considered and CB dose during inspirium should be calculated in order to make sure that the dose was kept within tolerance limits. Maximum CB dose in I phase was violated for 6 out of 10 patients according to our in-house protocol. However, mean CB doses were within limits in all but one of the patients and for all phases of the respiration.

Reported exposed CB dose for 4600- 5000 cGy whole breast irradiation was 153-650cGy (21, 22, 23). This dose is about 2-8% of the prescription dose and depends on several factors including the radiation technique and the energy. Previously, it was shown that dynamic intensity modulated radiation therapy (IMRT) technique caused more radiation exposure dose on CB when compared to 3 dimensional conformal techniques while static IMRT could reduce exposed CB dose (24, 25). Planning techniques used in this study were either 3 dimensional conformal RT or IMRT and the achieved maximum and mean CB doses were lower than the values mentioned in these studies. Using half beam block leads to increase CB dose while decreasing the exposed lung dose (22). Exposed CB dose is affected by primary breast size (25) and chest

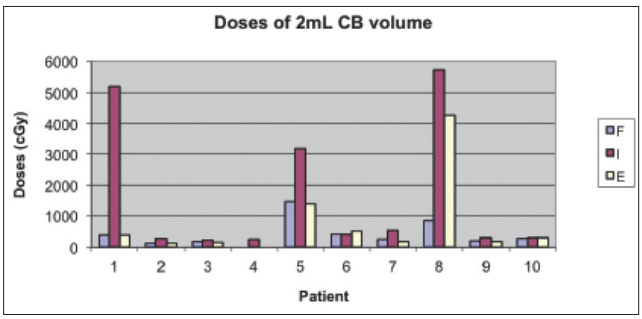


Figure 3. Changes in dose received by 2ml of the CB volume for each patient according to different phases of the breath cycle

wall irradiation results in less exposed dose compared to intact breast irradiation because of narrow tangential field size (21).

In English literature there are no studies examining the CB dose changes with breath cycle. However, there are several studies that reported decreased heart and lung doses for treatments delivered during I and respiratory gated RT gained wide acceptance for patients with left breast carcinoma (3, 4, 17). According to the results of this pilot study, CB doses calculated on images taken during F could not represent the whole respiration cycle.

Conclusion

Contralateral breast dose needs to be considered together with heart and lung dose changes during respiratory cycle because maximum CB dose could exceed the upper limit in 60% of patients during inspirium.

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