Romanian Reports in Physics **72**, 603 (2020)

# THE IMPACT OF BREAST IRRADIATION USING THERMOPLASTIC MASK ON TREATMENT DELIVERY AND ACUTE EFFECTS

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*Received January 24, 2020*

*Abstract*. Several methods of breast immobilisation exist for patients treated for left-sided breast carcinomas to reduce positioning errors and to limit dose to cardiac muscle. Thermoplastic masks are useful tools, particularly when respiratory-gated radiotherapy is not available. This study evaluates the impact of breast masks on treatment delivery and acute effects.

*Key words*: setup errors, radiotherapy, immobilising device.

## 1. INTRODUCTION

Breast cancer continues to be one of the most common neoplasms among women worldwide accounting for nearly 1 in 4 cancer cases, and the leading cause of cancer-related death [1]. Surgery, radiotherapy and chemotherapy are the standards of care, while targeted therapy and endocrine therapy can be employed on an individual basis, where treatments are available and/or recommended for an additional benefit to the patient. For resectable breast cancers, the current treatment standard consists of breast-conserving surgery followed by whole breast external beam radiotherapy [2]. Radiation therapy was shown to be an important component of the treatment process as it prevents local recurrence after breast-conserving surgery [3].

The aim of radiotherapy is to achieve a high therapeutic ratio by increasing tumour control *via* adequate target dosimetry and decreasing normal tissue toxicity through better protection of the organs at risk. To attain this goal, solutions are often required for treatment optimisation, such as the use of immobilising devices for setup error reduction. Rigid immobilisation of patients during radiotherapy to achieve accurate positioning of the target allows tumour margin reduction, which results not only in a decreased dose to healthy tissue but offers the potential to augment the dose to the target.

The materials and technology used today in radiotherapy departments allow immobilisation of nearly any area of the body. The effectiveness of various immobilisation systems/devices are commonly evaluated using portal imaging (2D information analysis) and CT (3D information analysis). While the head and neck regions are more common to be immobilised with rigid masks during radiotherapy, other parts of the body, such as the breasts, are among anatomical sites that greatly benefit from immobilising devices [4].

Over the years, the role of thermoplastic mask in patient immobilisation during breast irradiation became well known. For patients with large and pendulous breasts the prone setup represents the ideal solution for an accurate immobilisation, which can be achieved either with a designated board or using thermoplastic masks. There is, however, a scarcity of literature data regarding thermoplastic masks for breast immobilisation when no prone breast board is available.

Traditionally, breast cancer patients are positioned using permanent tattoos marked on the patient combined with the wall-laser system which is aligned to the linear accelerator. However, due to intra- and inter-fraction organ movement, this setup lacks accuracy, particularly for women with large breasts. In view of more reliable patient setup for positioning error reduction, various immobilising systems have been designed, such as the breast boards (supine or prone), still considered a standard technique [5]. A study undertaken by Barrett-Lennard and Thurston across 18 radiotherapy centres identified various (other than breast board) immobilisation devices including: thermoplastic mask, breast cups, wireless bra, Micropore tape, vacuum bags, plastic L-shaped supports, breast rings and stockings [6]. Notwithstanding the large number of possibilities, immobilisation is strongly patient-dependent and there is no one-fits-all system.

While deep inspiration breath hold is an excellent method of reducing heart dose for left-sided breast cancer patients [7], departments where this technique is not available (such as ours) can employ customised, thermoplastic masks as they offer a personalised-approach to patient positioning and are suitable for large breasted patients. Despite their advantages, these immobilising casts can have a build-up effect which augments the skin dose, thus leading to unwanted adverse events. Although most women undergoing radiation treatment for breast cancer experience a certain degree of radiation dermatitis, the addition of thermoplastic casts often add to these side effects, thus influencing the overall wellbeing and the quality of life of this patient group [8]. Patients receiving whole-breast radiotherapy usually undergo a course of 4–6 weeks treatment, with radiodermatitis being reported as the most common acute side effect [8]. There are several grading systems to assist the clinician to quantify acute radiation dermatitis: The Radiation Therapy Oncology Group (RTOG) / European Organization for Research and Treatment of Cancer (EORTC) toxicity criteria and the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTCAE) being the most commonly used [9, 10].

The aim of the current study was to assess the impact of breast irradiation using thermoplastic mask on treatment delivery and normal tissue side effects. The study focused on breast cancer patients with invasive left-sided breast carcinomas, as this patient group is more exposed to risk of cardiovascular disease due to unintentional irradiation of the cardiac muscle and its associated vasculature [11]. As concluded by the Early Breast Cancer Trialists' Collaborative Group, radiotherapy is demonstrably associated with excess mortality due to heart disease [12]. Therefore, reduction of setup errors through immobilisation could possibly improve treatment conformality and reduce the dose to adjacent normal structures.

## 2. METHODS

Patients with large breasts presenting with invasive left-sided breast carcinomas were treated post-segmentectomy with 3D conformal radiotherapy during the 2015–2018 time period, with a Siemens ARTISTE™ linear accelerator. The treatment protocol, correlated with tumour staging, consisted of breast-conserving surgery with/without chemotherapy and hormonal therapy.

Personalised thermoplastic masks were prepared to assist with immobilisation during fractionated radiotherapy. The study included 30 patients, between the ages of 35–59, where 15 patients were irradiated with the mask, while the other 15 underwent breast irradiation without immobilising masks, using breast boards with arm rest. Patient- and treatment-related characteristics are presented in Table 1.

*Table 1*

Patient and treatment-related characteristics

| Patient characteristics | Patients with mask | Patients without mask |
|---|---|---|
| Age in years (mean and range) | 42.8 (36 – 58) | 44.6 (35 – 59) |
| Side of breast | | |
| Left side | 15 (100%) | 15 (100%) |
| Right side | – | – |
| Breast volume ($cm^3$) (mean ± stdev) | 1405 ± 598 | 1171 ± 485 |
| Tumour staging | T1 – T3 | T1 – T3 |
| Chemotherapy | | |
| Neoadjuvant | 11 (73.3%) | 9 (60%) |
| Adjuvant | 6 (40%) | 4 (26.7%) |
| Surgery | 15 (100%) | 15 (100%) |
| Hormonal therapy | 15 (100%) | 15 (100%) |
| **Dosimetric parameters – CTV (tumour)** | | |
| Mean dose (Gy) ± stdev | 52.41 ± 1.13 | 51.91 ± 1.48 |
| D95 (Gy) ± stdev | 48.35 ± 0.93 | 47.11 ± 1.98 |
| D2 (Gy) ± stdev | 61.41 ± 4.58 | 58.65 ± 5.91 |
| **Dosimetric parameters – heart** | | |
| Mean heart dose ± stdev | 3.72 ± 1.68 | 3.61 ± 1.34 |
| D2 (Gy) ± stdev | 29.15 ± 14.42 | 34.4 ± 13.48 |

Dose prescriptions were identical for the two patient groups: 50 Gy in 25 fractions to the whole breast clinical target volume (CTV) and simultaneous integrated boost

(SIB) up to 60 Gy in 25 fractions. To retain the risk of cardiac mortality under 1%, the QUANTEC criteria was met by all treatment plans whereby the heart volume receiving 25 Gy (V25) should be kept below 10% (in 2 Gy fractions) [13]. Treatment plans have been completed within the medical physics department using the Isogray planning system.

The following main aspects were assessed in this study: (1) the reduction of setup errors with the immobilising mask; (2) the acute effects with/without the mask due to the build-up effect of the mask that can lead to an increased skin dose; patients' quality of life (QoL) during and post-radiotherapy.

The customized thermoplastic masks were moulded in the CT-SIM department (Fig. 1) by a process similar to the one involving head and neck immobilisation masks: the thermoplastic is immersed into a water bath heated up to 65–70°C for a few minutes, until is mouldable. After a brisk towel-drying, the mould is placed on the patient and left to allow it to harden completely. These masks offer the double advantage of reducing the positioning errors and eliminating the discomfort of subcutaneous tattoos normally required by the CT-SIM protocol. Each mask has the central axis marked, together with the lateral, longitudinal, and vertical alignment, according to the breast irradiation protocol. To note that these customised immobilising devices have been adapted from masks used in pelvic irradiation, therefore their rigidity is higher than the usual mesh-type thermoplastic used in breast irradiation. As a consequence, breast movement within the mask as well as mask deformation are negligible factors.

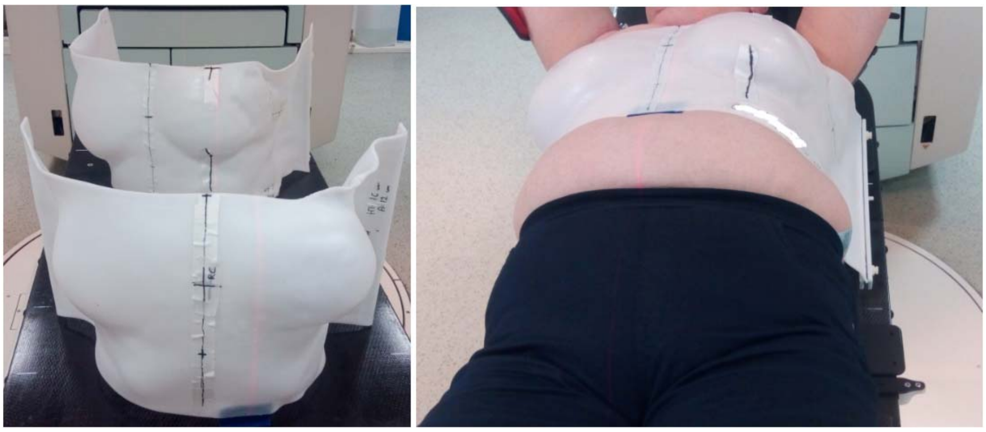

Fig. 1 – Image of in-house created thermoplastic masks (left) and patient setup with the immobilising mask (right).

Positioning (setup) errors were assessed by using the electronic portal imaging device (EPID). The setup errors were defined as the shifts of the landmarks along the *x*, *y* and *z* coordinates on the EPID film (based on anterior-posterior and lateral-

lateral orthogonal EPID images) from those on the digitally reconstructed radiograph (DRR) film. Patients were imaged on a weekly basis and in addition, whenever it was considered necessary by the therapist.

At the start of therapy, all patients signed a written informed consent for treatment, where all participants were informed about possible adverse events, particularly of radiodermatitis, as well as other risk factors (sun exposure, smoking, the use of inadequate ointments on the lesion), as well as the benefits of the treatment.

During the course of radiotherapy, patients were evaluated by their physician using both physical examination of the irradiated skin and verbal in-house questionnaire regarding QoL. The choice of verbal (instead of written) questionnaire for data collection was to provide a more personal, face-to-face experience between patient and physician / radiation therapist.

The main targeted aspects were:

(1) the grade and time interval to radiodermatitis,

(2) the impact of radiodermatitis on patient's quality of life.

Radiodermatitis was visually evaluated using the RTOG criteria [9]. According to the RTOG acute radiation morbidity criteria for skin, grade 1 toxicity includes dull erythema, epilation, dry desquamation and decreased sweating; grade 2: tender erythema, patchy moist desquamation and moderate edema; grade 3: confluent, moist desquamation other than skin folds, pitting edema and grade 4 includes ulceration, hemorrhage and necrosis.

In order to counteract the effects of grade 3 radiodermatitis, patients were advised by the physician to apply mercurochrome (a mercuric fluorescein derivative used as skin antiseptic) on the entire breast surface.

## 3. RESULTS

### 3.1. THE IMPACT OF THERMOPLASTIC MASK ON TREATMENT DELIVERY

To determine the setup errors, EPID images were overlapped with the DRR images for each patient. Weekly positioning errors were determined for the two patient groups along the $x$, $y$ and $z$ axes (Fig. 2). While the first two EPID measurements (first two treatment weeks) gave similar results in the two groups (around 1.3 mm), for the remaining treatment period, the mean error along the $x$ axis for patients wearing immobilising mask was $1.4 \pm 0.3$ mm, whereas for those without breast mask increased to $3.3 \pm 1.1$ mm. The same trend was seen along the other two directions. Overall, the results indicated a clear advantage of the thermoplastic mask in reducing setup errors to one third of the no-mask scenario. Furthermore, while the setup errors over the first two treatment weeks in both groups ranged between 1 and 2 mm, after the third week of treatment the errors in the no-mask group started to increase, reaching 4 mm. The immobilised group presented no changes. These errors, if not corrected, could pose long-term risks to the heart.

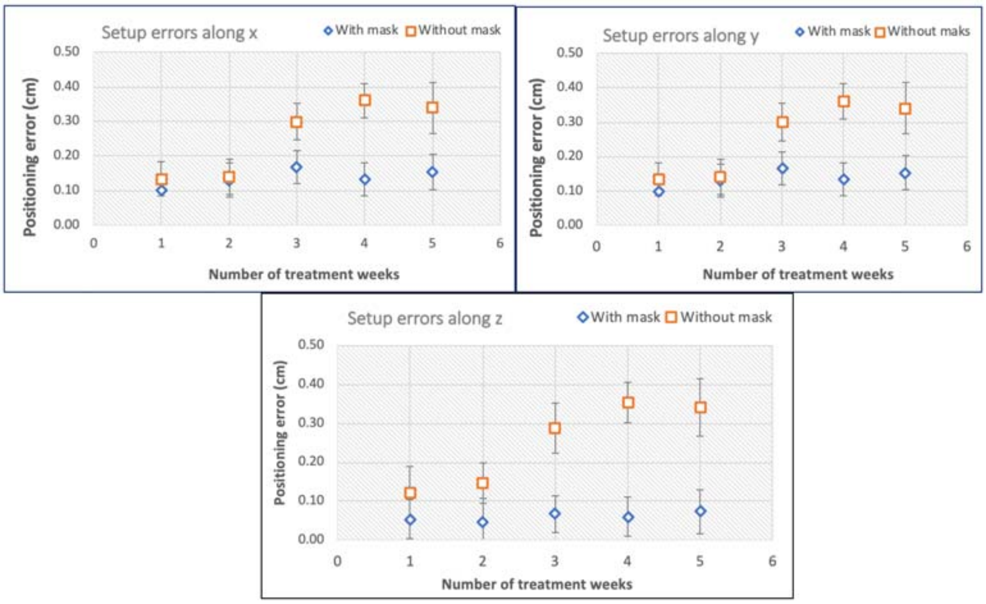


Fig. 2 – Setup errors along the *x*, *y* and *z* axis.

### 3.2. THE IMPACT OF THERMOPLASTIC MASK ON THE INCIDENCE OF ADVERSE SKIN REACTIONS

Acute skin effects were different in the two patient groups due to the increased dose to the skin surface caused by the addition of the plastic cast (in the group treated with the immobilising mask) that acted similar to a bolus. The group treated without the thermoplastic mask developed skin erythema after 10–14 days from the start of treatment, while all patients developed grade 1–2 radiodermatitis by the end of therapy (week 5). When irradiated with the thermoplastic mask, skin erythema was installed earlier, after the 7$^{th}$ day of treatment.

Grade 1 radiodermatitis in these patients appeared after 26–30 Gy. The radiodermatitis created an increased discomfort to the patients, as it locally amplified in intensity. By the 4$^{th}$ treatment week grade 2 radiodermatitis was present in the whole group (Fig. 3). All patients received analgesic, non-steroidal anti-inflammatory treatment and antibiotics to prevent acute skin infections.

By the end of treatment, 12 patients (80%) developed grade 3 radiodermatitis. Figure 3 represents the incidence of acute skin effects in the two patient groups:

those treated with the immobilising device (Fig. 3a) and those treated without mask (Fig. 3b).

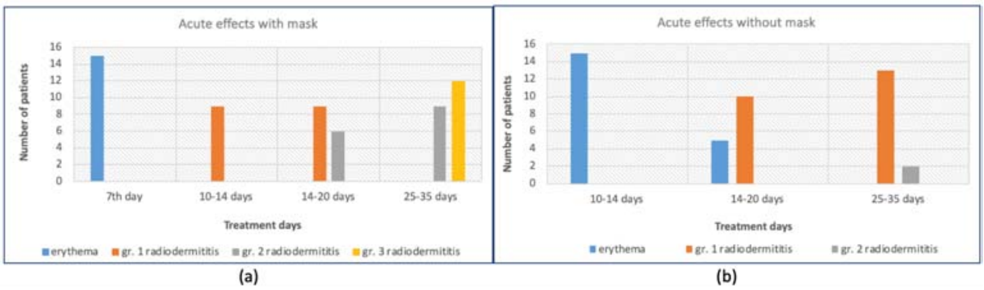


Fig. 3 – The incidence of acute effects during radiotherapy in patients immobilised with the thermoplastic mask (a) and in patients without immobilising mask (b).

### 3.3. THE IMPACT OF THERMOPLASTIC MASK ON PATIENTS' QUALITY OF LIFE

The QoL was directly proportional to the initiation of radiodermatitis. Local discomfort lead to insomnia, anxiety and mild depression, with more pronounced depressive episodes in women aged 35–40 years. Five patients presented with skin telangiectasia. Figure 3 illustrates the reported adverse events during radiotherapy in both patient groups. Those treated with the aid of the thermoplastic mask (Fig. 4a) reported a higher incidence and a greater spectrum of side effects compared to those patients that were not immobilised with the mask (Fig. 4b).

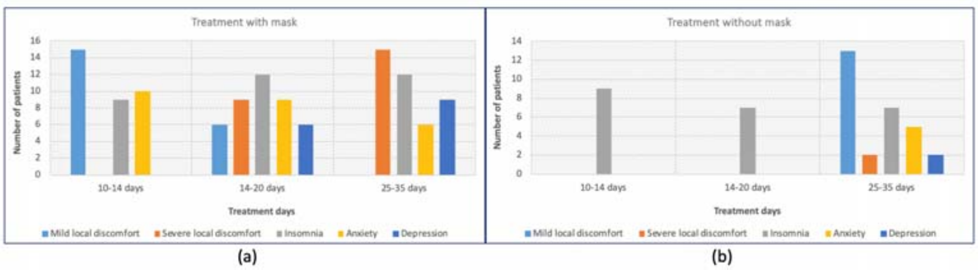


Fig. 4 – Radiotherapy-related adverse events in patients treated with immobilisation mask (a) and in patients treated without immobilisation mask (b).

While irradiation-induced fatigue together with the above adverse events decreased their QoL on the short term, 6-month post-therapy radiodermatitis has cleared, leaving only a light depigmentation on the breast skin. During patient follow-up, visible improvements of acute skin effects were noted. Figure 5 shows the positive evolution of the skin during the weeks following radiotherapy.

(a) (b)

Fig. 5 – The evolution of breast skin healing after radiotherapy using thermoplastic mask (a – 2 weeks after treatment completion; b – 2 months after treatment completion).

## 4. DISCUSSION

The role of immobilising casts and masks in radiation therapy is well documented and it has been evaluated within numerous clinical studies. It is known that in order to increase treatment precision and reproducibility during fractionated radiotherapy, immobilising devices play a critical role. While currently there are various techniques employed by radiotherapy departments to confine targeted body parts for a precise treatment delivery, certain devices used for immobilisation can cause adverse reactions.

The current report is based on a study that evaluated differences in setup reproducibility and acute toxicities in a group of 30 patients treated with 3D conformal radiotherapy for invasive left-sided breast carcinomas with or without immobilising breast mask. Weekly evaluation of positioning errors for the two patient groups along the $x$, $y$ and $z$ axes indicated a clear advantage of the thermoplastic mask, which has reduced the errors to one third of the no-mask scenario. While small shifts (below 2 mm) were seen in the group wearing the breast mask, these shifts were constant throughout the treatment, indicating a very good reproducibility of patient positioning. In the control group, these shifts reached 5 mm by the $4^{th}$ treatment week, thus strongly justifying the regular use of EPID images for setup corrections.

While the use of EPID for setup corrections of moving organs and tumours is highly needed, daily EPID imaging can be time consuming with high patient throughput, which certain departments cannot afford. In situations when weekly EPIDs are performed, immobilising masks are valuable ways to reduce inter-fraction setup errors, such in the current work. Furthermore, the lack of deep inspiration breath hold (DIBH) technique availability, which is an acknowledged method of reducing heart dose for left-sided breast cancer patients, makes thermoplastic masks suitable candidates for protecting the organs at risk through breast immobilisation.

Reports on the use of thermoplastic mask for breast immobilisation in the scientific literature are scarce, nevertheless the results generally show good reproducibility and reduction in organ movement. With the aim to review geometrical errors on portal localization films, Valdagni *et al.* have undertaken a study on 20 patients with early breast cancer after breast-conserving surgery [14]. All patients were immobilised with customized breast masks made of cellulose acetate, achieving good reproducibility. The positioning precisions reported by the study include a mean ventro-dorsal shift of 2.7 mm (on medial films) and 3 mm (on lateral films), and smaller cranio-caudal shifts on both medial films (1.8 mm) and lateral films (2 mm). In 15% of cases new masks were designed due to variations in breast morphology during treatment.

Another evaluation of positioning outcome with plastic masks for immobilisation was reported by Creutzberg *et al.* [15]. The study included 31 breast cancer patients treated with tangential beams. Seventeen patients were treated without a breast board but using plastic immobilisation of the breast, while the remaining 14 were treated without fixation (either flat or using an inclined breast board). The study showed that ventro-dorsal shifts were smaller when immobilisation was used (3.2 mm *vs* 4.6 mm). Furthermore, positioning reproducibility with the use of plastic mask was 3 mm in the ventro-dorsal direction, and was deemed acceptable. However, shifts along other directions were greater, due to difficulties in daily repositioning of the breast within the mask.

Using a repeated-measures design, Zierhut *et al.* investigated the use of thermoplastic immobilisation in 7 breast cancer patients in order to evaluate setup differences with and without the thermoplastic mask [16]. In their setting, the immobilisation device placed over the breast was attached to the breast board. Evaluation of setup errors with the thermoplastic mask indicated a mean ventro-dorsal shift of 0.3 cm +/– 0.29 cm, and a caudo-cephalic shift of 0.41 cm +/– 0.53 cm. The increase in skin dose was 17% due to the thermoplastic mask (from 47% without mask to 64% when using the thermoplastic). Maximum skin reaction in the form of dry desquamation was reported in 6 patients (86%) and moist desquamation in 1 patient. Evaluation of the cosmetic outcome at 1.5 years post-treatment was described as good, though no indication of the assessment method was given.

A more recent study on the effect of a thermoplastic immobilisation device on minimising breast or chest wall movement during radiotherapy was reported by Strydhorst *et al.* [17]. The study included 8 patients (5 patients with mastectomy and 3 with local excision) undergoing tomotherapy. It was shown that in 7 out of 8 patients, the immobilising device restricted intra-fraction motion in the anterior-posterior direction below 2 mm. However, this study had no control group, which makes it difficult to draw conclusions on the effectiveness of immobilising devices. Also, it could be suggested that positioning (and reproduction of positioning) of mastectomy patients is more facile than (re)positioning of patients that undergone local excision. Overall, differences in patients' characteristics between Strydhorst's study and our patient group (which did not include mastectomy patients) hinders an unbiased comparison.

One of the risk factors responsible for increased acute skin toxicity is the breast size, as patients with large breasts were shown to have a higher incidence of radiation-induced skin reactions [18, 19]. Furthermore, patients with high body mass index (BMI) have been associated with increased risk of acute reactions, including moist desquamation [20]. The above-presented studies lack information on patient characteristics regarding breast volume (or size). Recording the size of the breast in the context of immobilisation could possibly offer more insight into patient stratification, to identify the subgroup that would benefit the most from immobilisation with customised breast mask. In our study, the patients enrolled in the immobilised group had a mean breast volume of 1405 $cm^3$ with a median value of 1488 $cm^3$, whereas the group without immobilising device had a mean breast volume of 1171 $cm^3$ with a median of 1209 $cm^3$. While the initial dosimetric parameters between the two groups were similar (see Table 1) both regarding tumour coverage and the dose to the organs at risk (heart), organ motion during treatment can lead to dosimetric changes that affect the surrounding critical organs. While it is not a straightforward exercise to determine the actual dose received, it has been shown that setup errors larger than 3 mm in the posterior direction can lead to considerably increased dose to the heart [21]. Furthermore, the risk of heart and coronary disease increases between 4 and 7% with each 1 Gy in mean heart dose [22], creating the need for heart dose reduction a vital requirement. In our study, the setup errors due to patient positioning and organ motion over the 5 weeks treatment were smaller and more constant in the immobilised group as compared to the group without breast mask, where the setup errors had a threefold increase by the end of therapy.

## 5. CONCLUSIONS

Positioning errors during fractionated radiotherapy are often a challenge when treating large-breasted patients particularly with left-sided breast carcinomas. This is owing to the fact that after 15–20 dose fractions the inflammatory processes can change the shape of the breast, thus the initial position of the tumour. Furthermore, the proximity of the heart can increase the dose to the cardiac muscle leading to long-term adverse events. The use of breast masks was shown to considerably increase the reproducibility of patient positioning, limit the setup errors while offering an adequate protection to the heart.

A shortcoming of the thermoplastic mask is the increase in the skin dose, which resulted in grade 3 radiodermatitis in 80% of the immobilised patients. The impact of adverse effects on QoL can be diminished with the supportive care of the radiation therapists and physicians, showing that the use of thermoplastic mask outweighs the risk of deterministic skin effects.

***Acknowledgements.*** The authors would like to thank Mrs. Magdalena Boros and Mr. Szabolcs Szasz for their technical contribution to this study.

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