Technical Innovations & Patient Support in Radiation Oncology 7 (2018) 20–25

Contents lists available at ScienceDirect

Technical Innovations & Patient Support in Radiation Oncology

journal homepage: www.elsevier.com/locate/tipsro

Research article

Breast cancer patients report reduced sensitivity and pain using a barrier film during radiotherapy – A Danish intra-patient randomized multicentre study

Pia Krause Møller [a,b,*], Karina Olling [c], Martin Berg [d], Inger Habæk [a], Bente Haislund [e], Anne-Mette Iversen [f], Marianne Ewertz [a,g], Ebbe L. Lorenzen [a], Carsten Brink [a,g]

[a] Department of Oncology, Odense University Hospital, Denmark
[b] OPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark
[c] Department of Oncology, Vejle Hospital, Denmark
[d] Department of Medical Physics, Vejle Hospital, Denmark
[e] Department of Oncology, Herning Hospital, Denmark
[f] Department of Oncology, Århus University Hospital, Denmark
[g] Institute of Clinical Research, University of Southern Denmark, Denmark

ARTICLE INFO

Article history:
Received 22 December 2017
Received in revised form 22 April 2018
Accepted 10 May 2018

Keywords:
Breast cancer
PRO
Radiotherapy
Mepitel film
Radiodermatitis

ABSTRACT

Background and Purpose: Radiodermatitis is a well-known toxicity of radiotherapy and barrier film has been shown to reduce the severity of radiodermatitis. We have validated prior findings in a Danish cohort, using a similar barrier film and patient reported outcomes.
Materials and Methods: 101 Danish breast cancer patients were included at three radiotherapy centres. Based on randomization either the lateral or medial part of their chest was covered by Mepitel film; making the patients their own control. The primary endpoint was patient reported symptoms and experience. A secondary endpoint was radiotherapy staff evaluation of dermatitis.
Results: Within the skin area covered by film, the patients reported a statistical significant lower level of pain ($p < .001$), itching ($p = 0.005$), burning sensation ($p = 0.005$) as well as edema (p = 0.017) and reduced sensitivity ($p < .001$). Most patients (76%) would have preferred film on the entire treatment area ($p < 0.001$) and Mepitel Film as a standard treatment option (84%) ($p < 0.001$). Patients treated after mastectomy had a significantly lower severity of radiation-induced dermatitis with film at the end of RT compared to standard care ($p = 0.005$). However, in the blinded staff evaluation, no significant differences were found at follow-up.
Conclusions: Patients reported reduced symptoms from the skin with Mepitel Film and the majority would have preferred film as a standard offer to cover their entire treatment area. Especially women treated after mastectomy had a significantly lower level of radiodermatitis and preferred the film over standard care.

Introduction

Radiodermatitis is a common acute normal tissue response to radiotherapy and the radiosensitivity of the skin is influenced by patient- and treatment related factors as well as physical dose factors [1]. It occurs during or shortly after completion of treatment due to the integumentary system response to exposure of ionizing radiation, which depletes stem cells from the basal layer of the epidermis [2]. Experienced pain and discomfort due to radiodermatitis makes it important to prevent and manage skin reactions [3]. In the past 10 years several studies have investigated preventive strategies with steroidal or non-steroidal topical treatments, oral systemic therapy, light emitting diode treatment (LED) and barrier film [3–8].

The use of a Safetac technology-based film (Mepitel Film, Mölnlycke Healthcare) to protect the skin during the course of radiotherapy was investigated in 2014. Unlike other semi-permeable dressings, the film can be used from the first day of

* Corresponding author at: Pia Krause Møller, Department of Radiation Therapy, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark.
E-mail address: Pia.Krause.Moeller@rsyd.dk (P.K. Møller).

https://doi.org/10.1016/j.tipsro.2018.05.004

radiotherapy, potentially stays on for weeks and the transparency allows skin reactions to be assessed without removing the film [9]. Herst et al. succeeded in reducing their rate of moist desquamation from 26% when treated with aqueous cream compared to 0% when treated with Mepitel Film (n = 78) [6,10]. A case study with 3 cases also reported improved patient experience and reductions of severe skin reactions [5].

CT-based treatment planning with IMRT (Intensity-Modulated Radiation Therapy) has resulted in more homogenous dose distributions [4,11]. Results from the Danish Breast Cancer Group (DBCG) HYPO protocol showed on that grade 2 dermatitis (on the scale of the Radiation Therapy Oncology Group (RTOG-scale)) in week 5 of radiotherapy was 24% when treated with 15 fractions (40 Gray) and 67% when treated with 25 fractions (50 Gray) compared to 64% in the Herst population (46% <45 Gy) [6,12]. Few studies have used patient-rated measures as a primary endpoint [13].

The primary endpoint of this Danish study was to investigate patient-reported symptoms related to radiodermatitis and to examine patient preferences using Mepitel Film during their treatment course compared to standard skin care. A secondary outcome was to validate the study of Herst in a Danish cohort with a lower incidence of severe radiodermatitis compared to the Herst et al population.

Materials and methods

Study design

The study was a multicentre trial with participation of three Danish hospitals: Aarhus University Hospital (Herning site), Vejle Hospital, and Odense University Hospital.

All patients had either the lateral or medial part of the treatment area covered by film based on a randomization; making the patients their own control. The randomization procedure was conducted by assigned radiotherapists (RTTs) at each hospital in the online system RedCap (Research Electronic Data Capture) provided by Odense Patient Data Explorative Network (OPEN). A block randomization was conducted stratifying for hospital to balance at each institution the number of patients having film applied at the medial or lateral part of the chest. The last follow-up was the 27th of April 2016.

Ethics

The study was approved by the Danish Data Protection Agency (no. 2008-58-0035) and the Regional Committees on Health Research Ethics for Southern Denmark (project-ID S-20150112). Oral and written informed consent was obtained before randomization.

Questionnaires

A questionnaire was developed as no available instruments covered all the preferred items for patient reported outcomes and experiences. The questionnaire consisted of four sections – two with patient-reported outcome measures (PROM) regarding skin symptoms, one section with patient-reported experience measures (PREM) related to the use and preference of the barrier film and finally a section for staff evaluation of dermatitis.

The PROM-questionnaire was developed guided by existing validated questionnaires [14,15]. The PREM-questionnaire consisted of seven questions regarding comfort and preferences and both questionnaires used a 4-Point Likert Scale. The questionnaires were paper-based and cognitively validated by 3 randomly chosen patients. The patients answered the questionnaires on the day of their final radiotherapy treatment and a similar one at the two-week follow-up.

Blinded skin grading

Grade of radiodermatitis on both sides of the chest was assessed mutually by two RTTs at the final treatment and at the two-week follow-up. The RTTs were not involved in the treatment course of the patients and had no knowledge of the randomized treatment. To perform a blinded grading the film was removed the day before the final treatment. Patient blinding was not possible since the film was visible to the patient.

For skin grading, the RTOG/EORTC scale (grade 0–4) was used as it was the scale used for skin assessment in the departments involved in the study [16].

Participants

All women referred to postoperative adjuvant radiotherapy for breast cancer from October 1st 2015 to February 29th 2016 at the three departments were offered participation. The exclusion criteria were lack of compliance, not understanding Danish or inclusion in the ongoing Danish HYPO PBI protocol. Also, the women had to consent to a two-week follow-up.

Statistics

Patient characteristics were summarized separately for women with breast irradiation and chest wall irradiation. Differences in the distribution of the variables between these two groups were compared by Pearson x^2 test, unpaired *t*-test and Wilcoxon rank-sum test and a significance level of the estimated P-values was chosen to be 0.05.

Descriptive statistics were made on patient-reported symptoms and they were compared using Wilcoxon signed-rank test (paired analyses). Subgroup analyses were performed of the distribution of severe pain and sensitivity according to type of surgery, total dose and adjuvant chemotherapy.

Patient-reported experiences were dichotomized and binomial tests were used to test the distribution of the observed positive and negative difference from the binomial distribution. Descriptive statistics and Wilcoxon signed-rank test were used to investigate the differences in radiodermatitis with or without Mepitel Film. The data was analyzed using Stata14.

Radiotherapy

Danish breast cancer patients are treated according to DBCG guidelines with loco-regional radiotherapy on linear accelerators using CT-based dose-planning and intensity modulated radiotherapy techniques (IMRT). Dose planning aimed at covering the residual breast/chest wall and regional lymph nodes with 95% and 90% of the prescribed dose, respectively. Regarding hotspots, the volume receiving more than 105% should be kept below 2% of the breast volume. For mastectomies the corresponding dose level was 107%. Absolute maximum dose should be 108% and 110% for hypo and normo fractionated RT, respectively.

Since March 2014 hypo-fractionated breast radiotherapy based on 40 Gy/15 fractions in 3 weeks has been standard therapy in Denmark to patients with an indication for breast only radiotherapy [17].

Information and application of film

Guidelines for digital data reporting, film application instructions and patient information were created to homogenize the