

Radiotherapy skin marking with lancets versus electric marking pen - Comfort, satisfaction, effectiveness and cosmesis results from the randomized, double-blind COMFORTATTOO trial

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ABSTRACT

Introduction: Set-up skin markings are performed, in several centers, for radiotherapy (RT) treatments. This study aimed to compare two permanent methods: lancets and an electric marking pen, the Comfort Marker 2.0® (CM).

Methods: This was a prospective, unicentric, randomized study. Patients aged 18 years or older referred to our department to receive RT were recruited. Patients were randomly assigned, in a 1:1 ratio, to receive set-up markings using lancets or CM. The markings arrangement followed our departmental protocols. The coprimaries endpoints were patients' comfort and effectiveness. Secondary endpoints included radiation therapists (RTTs) satisfaction and cosmesis.

Results: Between October 2021 and January 2022, 100 patients were enrolled (50 received lancets and 50 CM) and assessed for the comfort and satisfaction outcomes. CM was significantly less painful than the lancets, with 44% and 16% of the patients, respectively, considering the tattooing process painless (RR = 2.75; 95% CI: 1.36 - 5.58). On the RTT-reported satisfaction, CM had significantly easier processes than lancets (98.0% vs. 78.0%, respectively; RR = 1.26; 95% CI: 1.08 - 1.46). For effectiveness and cosmesis assessment, 98 patients were analyzed (48 received lancets and 50 CM). Patients receiving CM had a significantly higher proportion of markings graded as good and excellent compared to those receiving lancets (98.0% and 50.0%, respectively, had $\geq 75\%$ of the tattoos assessed as good/excellent, RR = 1.96; 95% CI: 1.47 - 2.61). On the cosmetic evaluation, patients receiving CM had significantly better cosmetic markings, with a median score of 4.4 (vs. 3.5 for lancets, $p < 0.001$).

Conclusion: The trial results demonstrated that tattooing with the CM is significantly less painful, more effective, easier to apply, and cosmetically superior to tattooing with lancets.

Implications for practice: Tattooing with CM allows for better results regarding pain, quality, ease and cosmesis.

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Introduction

In the modern era of conformal radiation therapy (RT), patient skin markings are performed, in several radiation oncology centres, at the time of simulation for target localization.^{1,2} These play a crucial role during the course of RT, to achieve the set-up

reproducibility and the accuracy of treatment delivery. Different methods are used for this purpose, both permanent and non-permanent.^{3–5}

Permanent dark-ink tattooing is the most popular method across most RT departments.⁶ A non-toxic ink is injected into the skin layers using a disposable needle to make a millimetric permanent tattoo, that providing a reference mark on the skin. The location and number of the set-up tattoos vary depending on the anatomical area to be treated, and differ between radiotherapy centres, based on the protocol each institution adopted. Allergy,⁷ infection,⁸ and sharp injuries² are potential but infrequent

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hazards associated with tattooing, with only a few reports described in the literature. To address the cosmetic issues with dark ink tattoos, there has been research into using ultraviolet ink, that allows the tattoos to become undetectable in ambient lighting, without compromising the setup accuracy.^{9,10} Besides permanent tattooing, alternatives include the use of semi-permanent methods, such as henna ink, temporary tattoo seals, and oil-based pens.^{3–5,11} However, these methods are inferior to dark-ink markings in terms of patient comfort, durability, and longevity.^{4,12} Clinical practice is evolving to a mark-free RT, with the development of surface-guided systems, called SGRT, that allows to reduce or even completely obliterate the need for set-up skin markings,¹³ with comparable or even improvement set-up accuracy.^{6,14,15} For centres that are not equipped, yet, with SGRT systems, the skin markings remain essential for set-up.

Of the several methods for permanent tattooing dark-ink set-up markings, this study compares two of them: disposable lancets, and an electric marking pen, the Comfort Marker 2.0® (CM). These two methods were chosen due to the paucity of data comparing them, so we could accurately evaluate the advantages of transitioning from using the lancets to the CM as standard practice in our department.

The skin acts as a complex sensory organ. Typically, permanent marking is associated with a variable degree of pain, depending on some factors including the depth of the needle insertion.⁴ This unpleasant pain sensation during tattooing is linked to the presence of nociceptors that innervate our skin, which is different depending on the skin layer.¹⁶ Besides that, different tattooing methods produce visually distinct tattoos, which has some implications both concerning cosmesis and treatment set-up. While an acceptable cosmetic outcome affects the patient experience and satisfaction regarding the oncological treatment,^{17,18} the visual quality of the markings used on the patient alignment is key in terms of safety and treatment accuracy. The quality of the delivered treatments is dependent on the ability to position the patient accurately and reproducibly throughout the RT,¹³ and that requires visible and decent quality markings.

This study aimed to establish whether the use of CM translates into a benefit in terms of comfort, satisfaction, effectiveness, and cosmesis. COMFORTATTOO is the first trial to address such parameters.

Methods

Study design

This was a prospective, unicentric, randomized, controlled, parallel, cohort study conducted at a radiation therapy department in northern Portugal.

Patients

Eligible patients were adults aged at least 18 years and referred to our department to receive external beam RT. Additional inclusion criteria included an Eastern Cooperative Oncology Group performance status of 0–1, and an estimated fractionating schedule of at least 20 once-daily fractions. A latter protocol amendment allowed for patients with a minimum treatment of 13 fractions to be included. Patients requiring either immobilization thermoplastic masks (for head or head and shoulders) or vacuum cushion were excluded. No limit on the maximum number of cutaneous reference points was specified.

All patients provided written informed consent. The study was approved by our local ethics committees (Ethics Committee for

Health decision number CES 212/021) and the study was performed in accordance with the International Conference on Harmonization Guidelines on Good Clinical Practice and the Declaration of Helsinki.

Randomization and blinding

Patients were randomly assigned in a 1:1 ratio to receive skin set-up markings either using disposable lancets (control group) or an electric marking device, the Comfort Marker 2.0® (experimental group). Eligible patients were randomized via computer-generated random permuted blocks (block sizes of 10), stratified by the number of set-up markings (≤ 4 vs. >4). Treatment allocation was blinded to patients and to the radiation therapists (RTTs) presented in the treating rooms but was not possible for the RTTs presented in the CT simulation rooms.

CT simulation and set-up skin marking

The set-up markings were created during the simulation session. All patients underwent a CT simulation, where they were placed on the CT couch in the same position as the daily treatment. Once the CT was acquired, the final number of set-up markings required was established, and patients were randomized and received the skin markings with the allocated method. The patients' position, immobilization, and marking arrangement were standardized according to the irradiated area and followed our departmental protocols. Typically, patients received 4 to 5 cutaneous reference points, except for the patients that irradiate breast or chest wall who received 9 (for free-breathing techniques) or 11 (for deep-inspiration techniques). A scheme of the number and location of the set-up markings is provided in the Supplementary Appendix (Fig. S1)

For the control group, patients' markings were tattooed using a 28-gauge disposable lancet. A droplet of India ink was placed on the exact spot to be tattooed, and the skin was pricked, with one small movement, with the needle of the lancet. This process was repeated for every marking. For the experimental group, patients were tattooed with an electric marking pen developed for set-up marking, the CM, designed by CIVCO Radiotherapy/Medical Precision B.V. Patients received the 0.2 mm deep applications with the brand-included black pigment. The procedure followed the brand recommendations: the black pigment was absorbed into the safety needle that was then pressed on the skin surface, at a 90-degree angle with the skin and with a 180-degree rotation twist movement of the pen. Same as previous, this process was repeated for every marking. In both methods, after cleaning the excess ink, if the tattooing was considered unsuccessful, the process was repeated. The patients' markings were performed by a team of RTTs specifically allocated to the CT simulation, which consisted of 11 members. All of them received practical training that certified them to use the CM.

Outcomes and assessments

Coprimary endpoints were patient comfort and effectiveness. Comfort was verbally assessed on the 11-point numeric pain scale, with 0 being “no pain” and 10 being “the worst pain imaginable.” As more than one reference point was tattooed, the patients were asked to give an overall score to the procedure. Treatment allocation was blinded to patients, as to minimize the potential for bias.

Effectiveness was assessed by the RTT team that delivered the daily fractions. Skin markings were individually evaluated at several time points, specifically at the first fraction, then every 5

fractions, and one last time in the last fraction of RT. These evaluations were scored on a 4-point graded scale (corresponding to bad, reasonable, good, and excellent), based on the subjective quality of the markings for patient set-up. Evaluation performed by the same RTT(s) was recommended, however not mandatory. RTTs were blinded to treatment allocation.

Secondary endpoints included RTTs' satisfaction and cosmetic outcome. In the satisfaction assessment, the RTT that executed the tattooing was asked to score the ease of the process on a three-point scale (easy, medium, and hard).

For the cosmetic outcome evaluation, a photographic assessment was performed. Every set-up marking was individually photographed on one of the last three days of treatment. All photographs were scored by 20 observers (both physicians and RTTs) blind to patient identity and treatment allocation, on a five-point scale (corresponding from bad to excellent cosmesis).

Additionally, data on sharps injuries was collected. Sharp injuries were considered any incident which causes the needle of the lancet or the CM to inadvertently penetrate the skin of the RTT performing the tattooing during any of the tattooing process (material assembly, tattooing, or sharps disposal).

The study was performed per the scheme presented in Fig. 1. A substudy assessing the fading of the skin markings after six months is ongoing.

Sample size

The target sample size was 100 patients (balanced allocation between groups).

Statistical methods

The current study was designed using intent-to-treat analysis with no patients excluded due to noncompliance.

Continuous variables were described by their median, minimum and maximum. Categorical variables were expressed as actual numbers (n) and percentages (%). Normal distribution was checked using Kolmogorov–Smirnov and Shapiro–Wilk tests. Our data didn't follow a normal distribution, so non-parametric tests were applied. Differences between groups were evaluated using Mann–Whitney U test for independent samples and Wilcoxon Signed Ranks test for related samples when comparing continuous variables, and Chi-squared or Fisher's exact tests when comparing categorical variables. Relative risks were calculated on the significant variables.

All tests of statistical significance were two-sided, and a P-value < 0.05 was considered significant. Data were analysed using IBM® SPSS® Statistics software, version 26.

The authors are solely responsible for the design and conduct of this study, all study analyses, and the drafting and editing of the manuscript and its final contents.

The trial is registered at [ClinicalTrials.gov](https://clinicaltrials.gov), number NCT05371795.

Role of the funding source

This work was supported by CIVCO Radiotherapy/Medical Precision B.V. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between October 2021 and January 2022, a total of 100 patients were enrolled (Fig. 2). After randomization, all patients received the allocated intervention: 50 assigned to lancets and 50 assigned to CM. These 100 patients were assessed for both the comfort and the satisfaction outcomes. Two patients didn't proceed to the effectiveness and the cosmesis assessment, thus a total of 98 patients were analysed for these outcomes (48 patients assigned to lancets and 50 to CM).

Baseline characteristics were well balanced between the two groups (Table 1). The median age of all patients was 61 years, and the majority were women (73.0%). The number of set-up markings was also well balanced: 64.0% of the patients in the lancets group and 68.0% of those in the CM group had received >4 set-up markings, with a median of 9 in both groups. Most of the patients included were referred to irradiate breast or chest wall (61.0%), followed by pelvis (22.0%) and thorax (11.0%).

Patients' comfort

The percentage of patients that graded the tattooing process as painless was significantly higher for patients receiving CM compared to lancets (44.0% vs. 16.0%, respectively; $p = 0.008$). This translates into a risk ratio of 2.75, in favour of the CM (Table 2). Fig. S2 in the Supplementary Appendix illustrates the distribution of the patients' assessed pain scores.

Effectiveness

There was no significant difference in time between tattooing and the first evaluation or tattooing and the second evaluation in the two groups (Table 1). Additionally, we found no need to repeat the set-up markings during the radiation treatment, on either group, due to their complete fade.

The tattoo quality assessment categories of good and excellent were combined for the analysis. Patients receiving CM had a significantly higher proportion of RTT-reported good and excellent quality markings compared to those receiving lancets (Table 3). This trend was repeated through all the timepoints. This translates into a risk ratio of 1.44, 1.96 and 1.96, respectively. The distribution

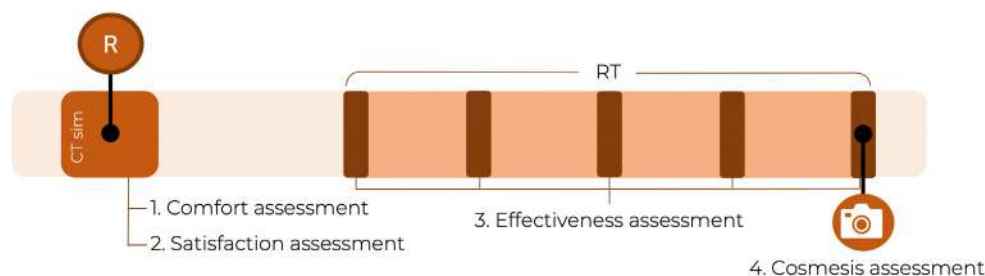


Figure 1. Overall study scheme. CTsim – CT simulation; R – randomization; RT – radiotherapy.

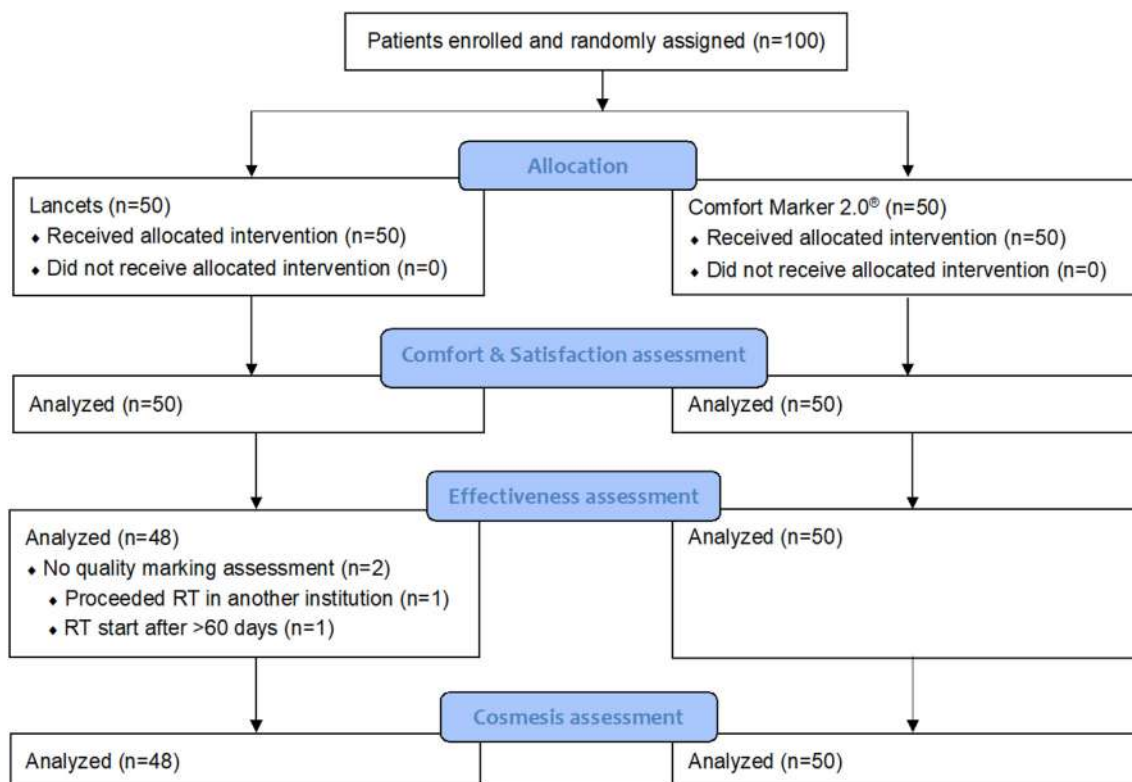


Figure 2. COMFORTATTOO trial profile.

of the RTTs' assessed quality markings is provided in the Supplementary Appendix (Fig. S4).

The median score of set-up markings graded as good/excellent on the last evaluation compared to the first was significantly worse in patients receiving lancets (67% v 89% respectively; $p = 0.003$). The same effect wasn't found on patients receiving CM (100.0% for both evaluations; $p = 0.173$).

Satisfaction

Compared to those receiving lancets, patients receiving CM had significantly higher RTT-reported tattooing processes evaluated as easy (78.0% vs. 98.0%, respectively; $p = 0.008$), which translates into a RR of 1.256, in favour of the CM (Table 4).

Cosmesis

The mean scores attributed by the 20 observers for each patient were used for the analysis.

Patients receiving CM had a significantly higher score on the photographic assessment (Table 5), with a median score of 3.5 and 4.5 for the lancets and the CM group, respectively ($p < 0.001$). While 84.0% of the patients in the CM group had a mean score of at least 4, in the lancets group that number is five times lower (16.7%; $p < 0.001$). The photographs of two participants, one from each arm, are provided in Fig. 3.

The distribution of the cosmesis assessment scores is provided in the Supplementary Appendix (Fig. S3).

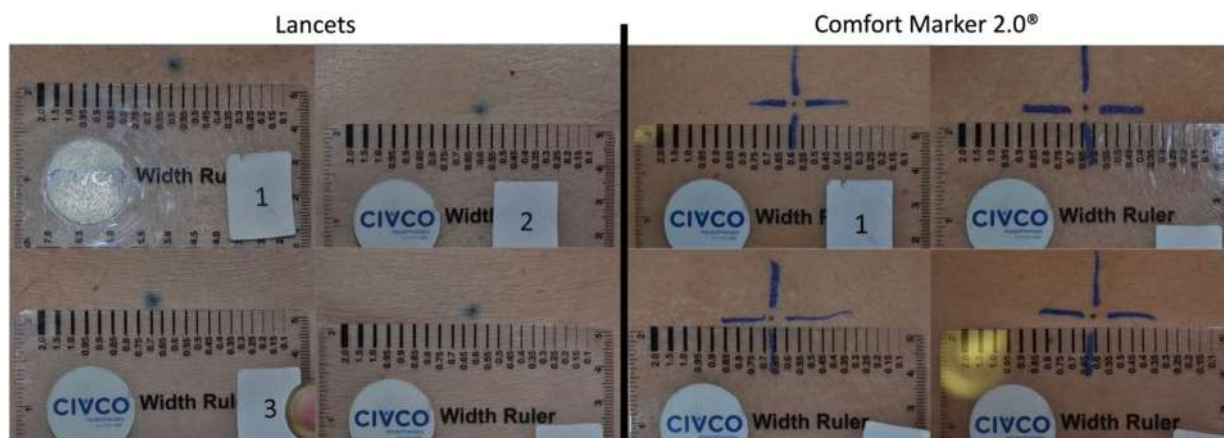


Figure 3. Individual photographs of the set-up markings recorded at the end of RT.

Table 1
Baseline demographic and clinical characteristics at randomization.

Variable	Total (N = 100)	Lancets (N = 50)	CM (N = 50)	p-value
Age (years)	61 (25–85)	63.5 (34–85)	58 (25–78)	0.135
Gender, n (%)				
Female	73 (73.0)	33 (66.0)	40 (80.0)	0.177
Male	27 (27.0)	17 (34.0)	10 (20.0)	
Irradiated area, n (%)				
Breast/Chest wall	61 (61.0)	28 (56.0)	33 (66.0)	0.127
Pelvis (±perineum)	22 (22.0)	9 (18.0)	13 (26.0)	
Thorax	11 (11.0)	9 (18.0)	2 (4.0)	
Abdomen	4 (4.0)	3 (6.0)	1 (2.0)	
Axilla	1 (1.0)	0 (0.0)	1 (2.0)	
Inguinal	1 (1.0)	1 (2.0)	0 (0.0)	
Nr of set-up markings, median (range)	9 (4–11)	9 (4–11)	9 (4–11)	0.229
≤4, n (%)	34 (34.0)	18 (36.0)	16 (32.0)	
>4, n (%)	66 (66.0)	32 (64.0)	34 (68.0)	0.833
Period between CTsim and RT start (days), median (range)	14.5 (6–51)	14 (6–51)	17 (7–48)	0.366
Period between CTsim and RT finish (days), median (range)	49 (26–80)	49 (26–80)	49 (34–77)	0.876

CTsim – computerized tomography simulation; RT – radiotherapy.

Table 2
Patients' pain assessments by study arm.

Variable	Lancets (N = 50)	CM (N = 50)	p-value	RR (CI 95%)
Pain assessment, median (range)	2 (0–9)	1 (0–6)	0.005	2.75 (1.36–5.58) ^a
0: no pain, n (%)	8 (16.0)	22 (44.0)	0.008	
1–2: mild pain, n (%)	26 (52.0)	19 (38.0)		
≥3: moderate/severe pain, n (%)	16 (32.0)	9 (18.0)		

P-values were calculated by Mann–Whitney U tests (two-sided). Lancet was the reference group when the relative risk (RR) was calculated. ^a RR for Pain = 0.

Table 3
Percentage of set up markings assessed as good and excellent by radiation therapists over three time points by study arm.

Tattoo quality	Lancets (N = 48)	CM (N = 50)	p-value	RR (CI 95%)
First evaluation, n (%)				
<75%	16 (33.3)	2 (4.0)	<0.001	1.44 (1.17–1.77) ^b
≥75%	32 (66.7)	48 (96.0)		
Last evaluation, n (%)				
<75%	25 (52.1)	3 (6.0)	<0.001	1.96 (1.45–2.66) ^b
≥75%	23 (47.9)	47 (94.0)		
All evaluations^a, n (%)				
<75%	24 (50.0)	1 (2.0)	<0.001	1.96 (1.47–2.61) ^b
≥75%	24 (50.0)	49 (98.0)		

Lancet was the reference group when the relative risk (RR) was calculated. ^b RR for ≥75%.

Table 4
Radiation therapists' satisfaction assessments by study arm.

Variable	Lancets (N = 50)	CM (N = 50)	p-value	RR (CI 95%)
Satisfaction assessment, n (%)				
Easy	39 (78.0)	49 (98.0)	0.008	1.26 (1.08–1.46) ^a
Medium	9 (18.0)	1 (2.0)		
Hard	2 (2.0)	0 (0.0)		

Lancet was the reference group when the relative risk (RR) was calculated. ^b RR for easy.

Table 5
Photographic cosmesis assessment by study arm.

	Lancets (N = 48)	CM (N = 50)	p-value	RR (CI 95%)
Median	3.5	4.4	<0.001	5.04 (2.65–9.60) ^a
<4	40 (83.3%)	8 (16.0%)	<0.001	
≥4	8 (16.7%)	42 (84.0%)		

Median was calculated on the mean scores attributed by the 20 observers for each patient. Lancet was the reference group when the relative risk (RR) was calculated. ^a RR for cosmesis ≥4.

Sharps injuries

No sharps injuries were registered.

Discussion

COMFORTATTOO is the first randomized trial to compare set-up skin tattooing with lancets to an electric marking pen. We demonstrated that tattooing the set-up markings with the Comfort Maker 2.0® revealed better in all the four outcomes assessed.

First, the use of the CM revealed to be significantly less painful than the lancets. 44.0% of the patients that received the former considered the procedure painless, whereas that was the case for 16.0% of the patients receiving lancets (RR = 2.75, 95% CI: 1.36–5.58). This difference might be explained by the difference in the needle insertion depth. The lancet needle is pricked on the skin with variable depth (1–4 mm), so it affects both the epidermis and the top layer of the dermis. On the other hand, the CM has a regulated mechanism of the pigment depth deposition that pricks only 0.2 mm, hence may not reach the dermis layer.¹⁹ As the nerve fibre density on the dermis is two to three times higher than the epidermis,²⁰ any stimulus that affects the dermis will produce a more painful event, which might explain our results. However, it must be noted this may be speculative and should be further investigated.

One additional challenge for RTTs is the identification of the tattoos. A faded mark represents an issue because patient positioning becomes more time-consuming, and it can even lead to possible set-up errors. Patients receiving CM had a significantly higher proportion of markings graded as good and excellent, whether in the first, the last, or in all evaluations combined. When combining all the assessments, while 98.0% of the patients in the CM group had at least three-quarters of the tattoos assessed as good/excellent, in the lancets group that number lowers to almost half (50%; RR = 1.96; 95% CI: 1.47–2.61). Furthermore, in the lancets

group there was a decrease in the quality of the tattoos over time, as patients reported significantly worse scores on the final evaluation than in the first evaluation (median of 88.9% of the markings graded as good/excellent on the first evaluation and 66.7% on the final evaluation; $p = 0.003$). This phenomenon may be related to the dynamic process of pigment deposition on the skin layers. The body reacts to the pigment as a foreign body. This originates a migration of immune system cells to the local to phagocytize the ink. Over time, the tattoo ink particles can be found to gradually move to the deeper dermis, which gives the tattoo a faded and blurred appearance.²¹ One possible explanation may, as stated previously, be related to the depth the ink is injected. The deeper the pigment is applied, the more expressive the foreign body reaction and the migration of phagocytes to the dermis is, which causes a faded and less noticeable marking.

The tattooing process with the CM was considered by the RTTs to be easier than with the lancets (98.0% of the processes were graded as easy vs. 78.0%, respectively; $RR = 1.26$, 95% CI: 1.08–1.46). However, this assessment was not masked, so the results must be interpreted with caution. Possible factors that explain this are the fact the ink is, instead of placed directly on the skin, absorbed into the safety needle so RTTs have a clear view of the field they will mark; and the need for fewer repeats due to unsuccessful tattooings.

Finally, on the photographic assessment, the CM had a better cosmetic result. While the CM group had a median score of 4.4, in the lancets group that score was 3.5 ($p < 0.001$). This result might, once again, be intrinsically associated with the depth of ink application, as we previously stated in their relation to the marking quality. The lancets tend to, over time, produce a more blurred and greenish marking, and that was graded by the evaluators as cosmetically unpleasant. On the other hand, the CM tattoos do not often fade or get the greenish halo, and tend to keep a round, uniform, with well-defined edges, and that's possibly considered cosmetically more pleasant. An acceptable cosmetic outcome is of importance.¹² Cosmesis interferes with the body perception patients experience after RT, as changes to physical appearance and body function are associated with poorer psychosocial outcomes, including depression and anxiety.^{17,18} This way, cosmetically better markings may ameliorate body image dissatisfaction and improve the patient experience.

COMFORTATTOO is the first randomized trial to compare two permanent marking systems, which limits the comparison with our results. Most papers available focus on the use of semi-permanent methods,^{3–5,11} with one study comparing semi-permanent to permanent marking. On this,⁴ although non-permanent approaches (marker pens and henna) allowed for less painful markings, they were associated with patient discomfort (as washings and bathing are not allowed due to the risk of complete fading) and the need for re-markings (mean of 10, 2 and 0 re-markings for marker pens, henna, and permanent marking, respectively, on 8–9 weeks long RT schemes). The permanent method used was similar to the lancets we used in our paper, which might explain the pain differences, that might be reduced using the CM, as we demonstrate in this paper. Although the study by Rafi does not evaluate the accuracy differences between the tested marking methods, the only study that compares semi-permanent and permanent skin marks found there are no differences in accuracy in the 351 breast cancer patients analysed.¹²

Another variable assessed by Rafi was the patient's satisfaction with body image. The authors recognized that dark-ink permanent markings impose a cosmetic problem for patients, which translates into a benefit for the non-permanent methods.⁴ This cosmetic concern led to the development of fluorescent-ink markings. A

few papers focusing on set-up accuracy are available, all reporting an interfraction reproducibility comparable with conventional dark ink.^{9,22} Only one paper assessed differences in body perception, and fluorescent-ink markings were associated with increased body image satisfaction scores.⁹ Again, these results cannot be directly compared to our study, and further investigation comparing dark-ink marking using CM and fluorescent-ink is needed.

Conclusion

In this randomized controlled trial, tattooing the set-up markings with the Comfort Maker 2.0® demonstrated to be significantly less painful, more effective, easier to apply, and produce cosmetically better markings compared to the use of lancets.

Conflict of interest statement

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.radi.2022.10.030>.

References

- Mukherji A. *Basics of planning and management of patients during radiation therapy*. 1 ed. Singapore: Springer; 2018. p. 403.
- Townend C, Landeg S, Thorne R, Kirby AM, McNair HA. A review of permanent marking for radiotherapy in the UK. *Radiography* 2020;**26**(1):9–14.
- Goto M, Oshiro Y, Tamaki Y, Ishida T, Kato Y, Shinoda K, et al. A novel method for skin marking in radiotherapy: first clinical use of temporary organic tattoo seal. *J Radiat Res* 2022;**63**(2):314–8.
- Rafi M, Tunio MA, Hashmi AH, Ahmed Z, editors. *Comparison of three methods for skin markings in conformal radiotherapy : temporary markers , and permanent Steritatt CIVCO A tattooing : patients@ comfort and radiographers satisfaction*; 2009.
- Wurstbauer K, Sedlmayer F, Kogelnik HD. Skin markings in external radiotherapy by temporary tattooing with henna: improvement of accuracy and increased patient comfort. *Int J Radiat Oncol Biol Phys* 2001;**50**(1):179–81.
- Rigley J, Robertson P, Scattergood L. Radiotherapy without tattoos: could this work? *Radiography* 2020;**26**(4):288–93.
- Sewak S, Graham P, Nankervis J. Tattoo allergy in patients receiving adjuvant radiotherapy for breast cancer. *Australas Radiol* 1999;**43**(4):558–61.
- Gilson RC, Pham CM, Gilson RT. Bullous *Pseudomonas* skin infection and bacteremia caused by tattoo ink used in radiation therapy. *JAAD Case Rep* 2015;**1**(4):222–4.
- Landeg SJ, Kirby AM, Lee SF, Bartlett F, Titmarsh K, Donovan E, et al. A randomized control trial evaluating fluorescent ink versus dark ink tattoos for breast radiotherapy. *Br J Radiol* 2016;**89**(1068):20160288.
- Lim LH, Pang EPP, Sultana R, Kusumawidjaja G, Wong RX, Yeo RMC, et al. A prospective randomized controlled trial to compare the use of conventional dark-ink tattoo and ultraviolet-ink tattoo for patients undergoing breast radiation therapy. *Pract Radiat Oncol* 2021;**11**(6):463–9.
- Ederer C, Sprenger A, Prokopetz M, Kofler LM, Wegmayr A, Lukas P. Hygienic aspects of marker pens in radiation therapy. *Strahlenther Onkol* 2018;**194**(9):861–3.
- Probst H, Dodwell D, Gray JC, Holmes M. An evaluation of the accuracy of semi-permanent skin marks for breast cancer irradiation. *Radiography* 2006;**12**(3):186–8.
- Naidoo W, Leech M. Feasibility of surface guided radiotherapy for patient positioning in breast radiotherapy versus conventional tattoo-based setups- a systematic review. *Tech Innov Patient Support Rad Oncol* 2022;**22**:39–49.
- Chang AJ, Zhao H, Wahab SH, Moore K, Taylor M, Zoberi I, et al. Video surface image guidance for external beam partial breast irradiation. *Pract Radiat Oncol* 2012;**2**(2):97–105.
- Shah AP, Dvorak T, Curry MS, Buchholz DJ, Meeks SL. Clinical evaluation of interfractional variations for whole breast radiotherapy using 3-dimensional surface imaging. *Pract Radiat Oncol* 2013;**3**(1):16–25.
- Shipton EA. Skin matters: identifying pain mechanisms and predicting treatment outcomes. *Neurol Res Int* 2013;**2013**:329364.
- Bregnhøj A, Hædersdal M. Q-switched YAG laser vs. punch biopsy excision for iatrogenic radiation tattoo markers – a randomized controlled trial. *J Eur Acad Dermatol Venereol* 2010;**24**(10):1183–6.

18. Fobair P, Stewart SL, Chang S, D'Onofrio C, Banks PJ, Bloom JR. Body image and sexual problems in young women with breast cancer. *Psycho Oncol* 2006;**15**(7): 579–94.
19. Oltulu P, Ince B, Kokbudak N, Findik S, Kilinc F. Measurement of epidermis, dermis, and total skin thicknesses from six different body regions with a new ethical histometric technique. *Turkish J Plastic Surg* 2018;**26**(2):56–61.
20. Schley M, Bayram A, Rukwied R, Dusch M, Konrad C, Benrath J, et al. Skin innervation at different depths correlates with small fibre function but not with pain in neuropathic pain patients. *Eur J Pain* 2012;**16**(10):1414–25.
21. Grant CA, Twigg PC, Baker R, Tobin DJ. Tattoo ink nanoparticles in skin tissue and fibroblasts. *Beilstein J Nanotechnol* 2015;**6**:1183–91.
22. David JE, Mossi K, editors. *Localization tattoos: an alternative method using fluorescent Inks*; 2006.