# What Is the Appropriate Skin Cleaning Method for Nasopharyngeal Cancer Radiotherapy Patients? a Randomized Controlled Trial

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# Abstract

**Purpose** To determine the effect of various cleaning methods for skin with acute radiation dermatitis (RD) in patients treated for nasopharyngeal carcinoma (NPC).

**Methods** A total of 168 NPC inpatients were randomized, while 152 patients completed the whole trial and the data were analyzed. Patients were randomly divided into non-washing group, washing with water alone group, and washing with water and soap group. All three groups received intensity modulated radiation therapy (IMRT) among other treatments. Follow-up from recruitment or the initial radiotherapy dose to 1 month after the final radiotherapy dose. CONSORT checklist was applied as the reporting guidelines for this study. Study evaluated a range of endpoints including incidence, timing, severity of acute RD and quality of life (QOL).

**Results** There were no allergic reactions or aggravating in both washing groups during the whole treatment. The incidence of acute RD was 100% in all three groups, while the degree of severity differed among groups. Washing moderately reduced severity compared with patients without washing; washing also delayed the onset time of acute RD, reduced the incidence of moist desquamation and pruritus. There were no significant difference among groups with respect to pain or burning sensation. Washing improved QOL on physical, emotional, and social functional dimensions. Washing with water and soap was the most effective on reducing itching and improving QOL among three groups.

**Conclusion** Washing irradiated skin reduces the occurrence and severity of acute radiation dermatitis.

**Clinical trial information** ChiCTR2000038231, date of registration 09.18.2020


# Introduction

Nasopharyngeal carcinoma (NPC) in China accounts for 38.29% and 40.14% of the worldwide morbidity and mortality of NPC, respectively. The associated morbidity and mortality are higher than the world average (1.2/10 million, 0.7/10 million), ranking 18th and 23rd in terms of incidence and mortality, respectively [1]. Radiation dermatitis is a kind of radiation damage to the epithelial and underlying structures of skin, which is characterized by erythema, dry or moist desquamation, and even ulcer [2]. The proportions of dry and moist desquamation were higher in patients receiving treatment to the head and neck than other diseases [3]. During radiotherapy, 90–95% of NPC patients suffer from acute radiation dermatitis. One-third to develop moist desquamation, causing substantial pain. Moist desquamation resulting from radical radiotherapy treatment was reported in more than 60% of patients [4]. The causes of the high incidence of RD of the neck skin include thinner skin, active sweat and sebaceous glands, more wrinkles, and frequent rubbing.

Because radiotherapy plays an important role in NPC treatment, RD occurs frequently. More patients and practitioners participate in skin cleaning during radiotherapy than ever before. Although both ONS [5] and MASCC [2] guidelines have been published to recommend skin washing as a way to maintain clean

irradiated skin. Nevertheless, there are a lot of questions for patients and healthcare professionals, such as “Can cleaning damage the skin? Is soap washing irritating?” What's more, evidence is controversy regarding the necessity to use mild soap during radiotherapy treatment [6]. Thus, some people are still conservative about cleaning.

Other than providing cleanliness and comfort, the effect of cleaning irradiated skin during radiation therapy is unclear. Only a few randomized trials aimed at this problem can be found in the literature. In a three-arm randomized trial of breast cancer patients treated with radiotherapy, less RD was observed in washing groups than in a non-washing group [7]. Another randomized controlled trial of breast cancer patients who received radiotherapy compared washing with water and soap and no washing [8], with the similar results. A clinical trial of patients receiving cranial radiotherapy found that the severity of RD was greater in a group that was not cleansed with shampoo [9]. But it is unclear whether it is safe or effective to clean irradiated skin during radiotherapy for NPC or patients receiving head and neck radiotherapy. Therefore, the objective of the present study was to determine the effects of washing irradiated skin with or without soap on acute RD and associated symptoms.

# Methods

### Study design

Three-arm prospective randomized controlled trial, as illustrating in Figure 1.

The study followed guidelines for reporting parallel group randomized trials [10], the CONSORT checklist as CONSORT guidelines was checked out (Supplementary File 1).

### Participants and setting

We enrolled patients with NPC who were transferred to the radiotherapy Center of Tianjin Medical University Cancer Institute and Hospital of China for initial radiotherapy from September 2020 to September 2021. All patients were inpatients and received IMRT.

Effective rate of moist desquamation incidence is the main outcome measure that we used to calculate the sample size. In a pilot study, 22% patients had moist desquamation in group 1, and 10% patients had it group 3. Therefore, the highest effective rate was 12%. The study was able to detect a 12% reduction in the incidence of moist desquamation. The power was 80% and the degree of significance alpha was 0.05 (one-sided test). To achieve this power, we needed 51 patients in each group. Considering a 10% loss to follow-up, we recruited 56 patients for each group. Before the start of the study, we set 168 as the sample size.

Before the beginning of radiotherapy, 168 patients were randomly divided into three groups: patients did not wash their skin during radiotherapy (group 1), patients washed with water (group 2), and patients washed with water and soap (group 3). The inclusion criteria were as follows: (a) NPC diagnosed with a definitive pathological report; (b) initially received radiotherapy on the head and neck, plans to receive

head and neck IMRT treatment with a total prescription dose of more than 60 Gy and a dose fraction of more than 28; (c) age >18 years; and (d) provision of written informed consent. The exclusion criteria were as follows: (a) diabetes or severe illnesses of the heart, liver, kidney, or hematopoietic system; (b) with skin ulceration or other skin diseases in the radiotherapy field; (c) communication disorder or mental illness; and (d) inability to be followed up.

The primary nurse in the ward is responsible for completing and supervising the cleaning methods of patients. There was no chance for patients in 3 different floors to communicate either in wards or in the radiotherapy rooms because their treatment time is assigned into different time intervals.

## Intervention

Potentially eligible patients were interviewed during the simulation or before the first treatment by two researchers for enrollment. Eligible patients were randomly allocated before starting radiotherapy by special nurse who only charged for assigning them to interventions. Before recruiting patients, the random allocation sequence was generated by specialist researchers in clinical trail center, who didn't participate the clinical work. The assignment numbers were placed into an opaque envelope only known by him. When a patient consented to participate in the study, the next patient number in chronological order was assigned to her and the corresponding envelope was unsealed, revealing assignment to one of the three groups. Patients were asked not to tell healthcare professionals or other patients which group they belonged to. For technical reasons, cleaning methods could not be blinded to the patients and the interveners. Therefore, only outcome measures were blind.

Patients used various cleaning methods for irradiated skin during radiotherapy: group 1 non-washing irradiated skin, group 2 gentle washing of irradiated skin with warm water (35–40℃) and group 3 gentle washing of irradiated skin with warm water (35–40℃) and mild soap (Dove®), followed by rinsing with water to remove residual soap. Patients in groups 2 and 3 were instructed to wash correctly but were not permitted to shower or bathe. Frequencies of cleaning in groups 2 and 3 were 2 or 3 times a day. The cleaning time should be at least half an hour removed from the radiotherapy time. Towels and Dove® Soap were provided by the researchers. Trained nurses from three different floors completed the intervention for the patients in that floor separately. Supportive Care Guidelines Group (2005) defines “mild” soap as a pH balanced product that does not contain lanolin. The Dove® Soap used in group 3 was low irritant, which was lanolin free and non-alkaline with the mild pH. What’s more, Dove® is the popular brand which is considered mild by the general public and may be used more frequently [6].

General recommendations for all three groups were as follows: (a) remove dentures, earrings, necklaces, and other metal products before radiotherapy to avoid increased radiation absorption; (b) consume a high-protein diet, with daily consumption of more than 2000ml water to reduce a systemic radiation response during radiotherapy; (c) wear loose soft cotton or silk clothing, and do not scratch the radiation field skin; and (d) avoid using deodorant, lotion, cream, perfume, cosmetics; avoid direct sunlight on the radiation field skin; avoid pasting medical dressings and using iodine, alcohol, or other irritating

disinfectants; avoid hot or cold stimulation, such as hot compresses and ice pack. The three groups were consistent in the use of skin protectants during radiotherapy.

All patients received IMRT with positioning under the simulator, resting on the head and neck, with a fixed mask and personalized lead blocks. IMRT was utilized to treat primary tumors to the dose of 2.12 Gy/fraction of 70 Gy and all regional lymph nodes were treated with the dose of 1.8 Gy/fraction to 60 Gy simultaneously. The following treatment measures may or may not be provided: (1) **Induction chemotherapy**: intravenous chemotherapy with TPF regimen before radiotherapy, docetaxel 80 mg/m$^2$ on day 1, cisplatin 80 mg/m$^2$ from days 1 to 3, and tegafur 1000 mg from days 2 to 6. There were two or three cycles before radiotherapy; (2) **Concurrent chemotherapy with cisplatin**: intravenous chemotherapy was performed on the first day of radiotherapy, and cisplatin was used as a single-drug chemotherapy at 80 mg/m$^2$, on days 1, 22, and 43; or (3) **Synchronous targeting therapy**: intravenous targeting therapy with nituzumab 200 mg once per week during radiotherapy.

## Measures

The main outcomes were the incidence of acute RD and moist desquamation, the secondary outcomes were the severity of subjective symptoms (pain, burning, itching) and QOL. RD and moist desquamation was scored by two principal authors according to the Chinese version [11] of the RTOG acute toxicity scale in the radiotherapy oncology group [12]. Two lead authors accountable for results evaluation were trained by the enterostomy therapist (ET) who had been certified internationally. When physicians did not agree on RD grade or whether moist desquamation occured, ruling by ET. RD and moist desquamation were assessed every day from the beginning of radiotherapy to 1 month after the completion of radiotherapy.

Because moist desquamation worsens quality of life (QOL), this was recorded separately. Before starting treatment, we used a questionnaire to record socio-demographic data. We recorded scores of pain, itching and burning using patient-reported outcome software every day, and we measured symptoms using a visual analogue scale (VAS). VAS is the international commonly used scale in pain or other subjective feelings, which reliability has been confirmed in China [13]. We used the maximal score of the symptoms to compare among three groups.

QOL was assessed at three time points for the Chinese version of EORTC QOL-C30 (V3.0) as an instrument at the beginning, the end and 1 month after the completion of radiotherapy. EORTC QOL-C30 is a cross-cultural quality of life measurement tool for cancer patients, which the Chinese version has been verified to have good reliability (Cronbach's alpha≥0.70) and validity (r>0.81) [14].

Socio-demographic data was computed with the use of a questionnaire before the beginning of treatment. Other data from this study included the type of cleaning, the frequency of cleaning, characteristics related to tumors and previous treatments, radiation techniques, treatment interruptions and adjuvant treatments. If we did not see a patient during the follow-up, they would receive a

questionnaire by email or written form by express delivery, and were required to replay photos of the irradiated skin through e-mail transmission.

### Statistical analysis

The chi-squared test was used to compare the frequency of RTOG acute toxicity severity in each group, as well as other categorical variables. We calculated differences in measured data (age, BMI, and patient-reported outcome symptom score) using analysis of variance. We set the significance level of $P<0.05$. All $P$ values were two-tailed.

## Results

Patients were enrolled from September 2020 to September 2021. A total of 256 patients with NPC were assessed for eligibility, of which 168 (65.6%) met the criteria and agreed to participate in the study. Of the 168 patients, 16 did not reach the end of the study and 152 patients were available for analysis **(Figure 1)**. There were 51 patients in group 1, 51 in group 2, and 50 in group 3. **Table 1** summarize the Baseline characteristics. As showing in **Table 2**, QOL were assessed before radiotherapy. ***There were no allergic reactions or other unsafe events in all 168 patients.***

**Table 3** shows there was a statistically significant difference in the severity of RD between the three groups ($P<0.001$). We set grades 0 and 1 as mild, and grades 2 and 3 as severe. With this grouping, severity of RD in three groups was statistically significant ($P=0.018$). These findings suggest that washing irradiated skin reduces the incidence of grades 2 and 3 acute RD. The differences in severity between groups 1 and 2 ($P=0.004$) and between groups 1 and 3 ($P<0.001$) were statistically significant. There was no significant difference between groups 2 and 3 ($P=0.625$). However, there was a decreasing trend toward the incidence of severe RD in the mild soap group. What's more, the differences in occurrence time of acute RD in the three groups were statistically significant ($P<0.001$). The occurrence of acute RD in group 1 was earlier than that of groups 2 ($P=0.001$) and 3 ($P<0.001$). There was no significant difference between groups 2 and 3 ($P=0.775$). This was provided in **Supplementary File 2** for the limit of table numbers.

**Table 4** shows there were significant differences in the presence of moist desquamation among the three groups during radiotherapy ($P=0.003$). The incidence of moist desquamation in group 1 was the highest ($P=0.006$ compared with group 2, $P=0.007$ compared with group 3), and there was no significant difference between groups 2 and 3 ($P=1.000$).

**Table 5** shows there were no significant differences in peak score of pain and burning among the three groups during radiotherapy ($P>0.05$). There was a significant difference in the itching peak score among the three groups ($P<0.001$). Peak score of itching among three groups ranked as following: group 1>group 2>group 3.

The data were evaluated at the end of radiotherapy and one month after radiotherapy with Chinese version of EORTC QLQ-C30 V3.0. Only five functional dimensions were listed by convenience. The item of pain was compared separately as the main subject symptom of RD. The other eight individual items (fatigue, nausea and vomiting, dyspnea, insomnia, anorexia, constipation, diarrhea and economic difficulties) showed no significant differences during the entire course of the study ($P$>0.05). So we compared five functional dimensions of QOL. **Table 2** shows there were significant differences in physical function, emotional function, and social function among three groups at the end of radiotherapy ($P$<0.05). We further compared the scores of the three groups, from high to low, as follows: group 3>group 2>group 1 ($P$<0.05). The outcome was similar at one month after radiotherapy ($P$<0.05).

# Discussion

IMRT was reported to reduce the incidence of RD effectively in breast cancer patients because of its accuracy [15-19], but in the present study, we showed that the incidence of acute RD was not significantly lower than that of conventional radiotherapy, same as other studies [20-23]. The absorbed dose of the head, neck, and shoulder fixed mask on the skin is higher than that of the unfixed mask [24]. The high incidence of acute RD in patients with NPC in our three-group study was due to the high radiation dose and the presence of superficial lymph node metastasis in most patients. Comprehensive therapy, radiotherapy combined with induction chemotherapy [21-22], concurrent and synchronous chemotherapy [22], and targeted therapy [23,25-26] all had synergistic effects on RD. Recovery from radiation adverse reactions is rare because of the effects of continuous use of anticancer drugs [27]. For these reasons, RD deserves long-term study.

We found that cleaning irradiated skin reduces the incidence of severe acute RD of grades 2 and 3. Compared with the non-washing group, washing with or without soap both reduced the incidence of grade 2 RD, consistent with the study [8]. In a study of head skin care of patients receiving whole skull radiotherapy, cleaning the skin did not increase the severity of acute radiation injury [9]. In the present study, the incidence of acute RD in groups 2 and 3 was significantly lower than group 1 during the first 20 fractions (cumulative radiation dose less than 42.4 Gy). These findings suggest that washing delays the occurrence of RD.

Cleaning reduces the number of bacteria on the surface of the skin and reduces the peeling and scraping caused by itching, enhancing the protective mechanism of epithelial cells, and reducing the stimulation of epithelial tissue caused by tissue compensation to radiotherapy. We showed that washing reduces itching and moisture desquamation, consistent with the studies [8], and the symptoms in soap group was lower than water group [7]. In our study, there was no significant difference in the incidence and perception of RD between groups 2 and 3. At the minimum, we demonstrated the safety of mild soap. Use of mild soap had different results in groups 2 and 3 in terms of itching and QOL. Washing with mild soap did not increase the incidence of RD or moist desquamation. This finding suggests that mild soap is friendly to the skin and there is no residual soap liquid on the skin if the patient uses the correct washing

technique. Next, we may try prolonging the contact time of mild soap on irradiated skin to explore the role of mild soap.

There has been a longstanding debate about whether irradiated skin can be cleaned in the irradiation field. If patients receiving radiotherapy are strictly restricted from washing, their normal hygiene and cleaning habits will be changed. Feelings of being dirty and offensive odors have negative impacts on QOL, psychological status and social functions [28]. Studies have shown that unlimited skin cleaning during radiotherapy can increase physical comfort and pleasure [29], encouraging patients to wash can reduce their anxiety and other adverse psychological emotions [30]. The effect of RD on QOL of patients is significant [31], especially for NPC, RD limited the head and neck movement of patients with NPC which severely affects self-image and self-esteem [32]. Cleaning irradiated skin can improve physiological and emotional and social functions of QOL.

Radiation reactions often exacerbate existing functional difficulties and may severely limit normal life [33]. Few studies examined what happens when radiotherapy ends. It was recommended to extend the intervention and observation time regarding acute and long-term toxicity following radiotherapy [34]. In our study, a considerable amount of dry desquamations occurred within 1 month after radiotherapy; fortunately, wet desquamations did not occur. The patients were instructed not to tear or pull the dry skin that had not been shed, so as to maintain the integrity of the skin, because maintaining the integrity of the skin has long been considered to be of great importance [29-30].

Washing irradiated skin is cost-effective. Pharmacological interventions were effective to prevent or treat RD in patients with head and neck cancer [35-38]. A systematic review concluded that topical interventions prevent acute RD in patients with head and neck cancer [39]. There was no strong evidence that indicated differences between topical pharmacological and non-pharmacological interventions (such as washing) in the prevention of acute RD. Obviously, washing irradiated skin is effective and economical.

The present study has some limitations. Firstly, the participants could not be blinded to skin cleaning treatment. Thus, positive changes in QOL may have partially resulted from the Hawthorne effect. Secondly, this study involved in one center, so larger scale RCT is needed.

To our knowledge, this is the first study providing the result of whether it is safe or effective for clean irradiated skin during radiotherapy for NPC or patients receiving head and neck radiotherapy. And this research may have an impact on prevention care of acute radiation dermatitis of diseases which have similar characteristics as irradiated skin has many skin wrinkles or the high dose of radiation regimen. It provides positive clinical evidence especially for some people still conservative about cleaning.

# Conclusion

In conclusion, washing irradiated skin with water or water and mild soap can reduce the severity of RD, delays its occurrence, reduces itching, and improves QOL. Patients should be encouraged to wash

irradiated skin correctly follow their cleansing habits with or without mild soap.

# Declarations


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### Author contributions

Study concept and design: Wanmin Qiang, Qingfen Zhang, and Ying Wang. Data acquisition: Qingfen Zhang, Ying Wang, Shuang Yang, and Qian Wu. Data analysis and interpretation: all authors. Writing review and editing: all authors. QFZ and YW are Co-first authors.


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### Data availability

Date that support the findings of this study are available from the corresponding author, upon reasonable request.

### Ethics approval

The study was approved by the Institutional Research Ethics Committee of our hospital (No. bc2019085). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

### Consent to participate

Informed consent was obtained from all individual participants included in the study.

### Consent for publication

N/A

### Conflict of interest

The authors declare no competing interest.

# References

1. Chen, W., Zheng, R., Zeng, H., Zhang, S., & He, J. (2015). Annual report on status of cancer in China, 2011. Chinese Journal of Cancer research, 27(1), 2–12. https://doi.org/10.3978/j.issn.1000-9604.2015.01.06
2. Wong, R. K., Bensadoun, R. J., Boers-Doets, C. B., Bryce, J., Chan, A., Epstein, J. B., Eaby-Sandy, B., & Lacouture, M. E. (2013). Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer, 21(10), 2933–2948. https://doi.org/10.1007/s00520-013-1896-2
3. Chan, R. J. (2019) What can we learn from researching in an overcrowded research area? Lessons learned from the 50 years of research on radiation dermatitis. Cancer Nursing, 42(5), 343–344. https://doi.org/10.1097/NCC.0000000000000739
4. Zhong, W. H., Tang, Q. F., Hu, L. Y., & Feng, H. X. (2013). Mepilex Lite dressings for managing acute radiation dermatitis in nasopharyngeal carcinoma patients: A systematic controlled clinical trial. Medical Oncology (Northwood, London, England), 30(4), 761. https://doi.org/10.1007/s12032-013-0761-y
5. Bruner, Deborah Watkins, Morilynl, et al.(2005). Manual for radiation oncology nursing practice and education. USA: Oncology Nursing Society.
6. Robertson K, Brown P. (2011). Mild soaps and radiotherapy: a survey of the UK public to identify brands of soap considered mild and analysis of these to ascertain suitability for recommendation in radiotherapy departments. Eur J Cancer Care (Engl), 20(3): 315-21. https://doi.org/10.1111/j.1365-2354.2010.01181.x
7. Campbell, I. R., & Illingworth, M. H. (1992). Can patients wash during radiotherapy to the breast or chest wall? A randomized controlled trial. Clinical Oncology (Royal College of Radiologists (Great Britain)), *4*(2), 78–82. https://doi.org/10.1016/s0936-6555(05)80971-9
8. Roy, I., Fortin, A., & Larochelle, M. (2001). The impact of skin washing with water and soap during breast irradiation: A randomized study. Radiother Oncol, 58(3), 333–339. https://doi.org/10.1016/s0167-8140(00)00322-4
9. Westbury, C., Hines, F., Hawkes, E., Ashley, S., & Brada, M. (2000). Advice on hair and scalp care during cranial radiotherapy: A prospective randomized trial. Radiother Oncol, 54(2), 109–116. https://doi.org/10.1016/s0167-8140(99)00146-2
10. Schulz, K. F., Altman, D. G., Moher, D., & the CONSORT Group. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med, 152(11), 726–732. https://doi.org/10.7326/0003-4819-152-11-201006010-00232
11. Wang., R.Z., & Fan., R.T. (2005). Radiation Oncology. Beijing: People's Medical Publishing House, 108-109.
12. Cox J D, Stetz J, Pajak T F. (1995). Toxicity criteria of the Radiation Therapy Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys, 31(5): 1341-1346. https://doi.org/10.1016/0360-3016(95)00060-C

13. Yuan., W., & Xiao., S.Y. (2013). Clinical application of pain assessment tool, Chinese Mental Health Journal, 27(5): 331-333https://doi.org/10.3969/j.issn.1000-6729.2013.05.003
14. Tan SS, Li H, Luo J, Chen NJ, Song Y, Jiang GL, & Yang FY. (2006). Assessment on the standard Chinese version of the quality of life core questionnaire version 3.0 designed by European Organization for Research and Treatment of Cancer. Zhongguo Linchuang Kangfu, 10(4): 23-27. https://doi.10.3321/j.issn:1673-8225.2006.04.006
15. Freedman, G. M., Anderson, P. R., Li, J., Eisenberg, D. F., Hanlon, A. L., Wang, L., & Nicolaou, N. (2006). Intensity modulated radiation therapy (IMRT) decreases acute skin toxicity for women receiving radiation for breast cancer. Am J Clin Oncol, 29(1), 66–70. https://doi.org/10.1097/01.coc.0000197661.09628.03
16. Freedman, G. M., Li, T., Nicolaou, N., Chen, Y., Ma, C. C., & Anderson, P. R. (2009). Breast intensity-modulated radiation therapy reduces time spent with acute dermatitis for women of all breast sizes during radiation. Int J Radiat Oncol Biol Phys, 74(3), 689–694. https://doi.org/10.1016/j.ijrobp.2008.08.071
17. Pignol, J. P., Olivotto, I., Rakovitch, E., Gardner, S., Sixel, K., Beckham, W., Vu, T. T., Truong, P., Ackerman, I., & Paszat, L. (2008). A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J* Clin Oncol, 26(13), 2085–2092. https://doi.org/10.1200/JCO.2007.15.2488
18. Kong, F., Ying, H., Huang, S., Du, C., Zhou, J., & Hu, C. (2014). Preliminary results of nasopharyngeal carcinoma treated with intensity-modulated radiotherapy: A retrospective study of 364 patients. Eur Arch Otorhinolaryngol, *2*71(12), 3283–3290. https://doi.org/10.1007/s00405-014-2900-2
19. Vergeer, M. R., Doornaert, P. A., Rietveld, D. H., Leemans, C. R., Slotman, B. J., & Langendijk, J. A. (2009). Intensity-modulated radiotherapy reduces radiation-induced morbidity and improves health-related quality of life: Results of a nonrandomized prospective study using a standardized follow-up program. Int J Radiat Oncol Biol Phys, 74(1), 1–8. https://doi.org/10.1016/j.ijrobp.2008.07.059
20. Ng, W. T., Lee, M. C., Hung, W. M., Choi, C. W., Lee, K. C., Chan, O. S., & Lee, A. W. (2011). Clinical outcomes and patterns of failure after intensity-modulated radiotherapy for nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys, 79(2), 420–428. https://doi.org/10.1016/j.ijrobp.2009.11.024
21. Huang, J. F., Zhang, F. Z., Zou, Q. Z., Zhou, L. Y., Yang, B., Chu, J. J., Yu, J. H., Zhang, H. W., Yuan, X. P., Tai, G. M., Liu, F. J., & Ma, C. C. (2017). Induction chemotherapy followed by concurrent chemoradiation and nimotuzumab for locoregionally advanced nasopharyngeal carcinoma: Preliminary results from a phase II clinical trial. Oncotarget, 8(2), 2457–2465. https://doi.org/10.18632/oncotarget.13899
22. Fan, T. Y., Xing, J., Lu, J., Liu, T. H., Xu, M., Zhang, Y. J., Shao, Q., Li, J. B., & Yu, J. M. (2013). Phase I/II study of induction chemotherapy plus concurrent chemotherapy and SMART-IMRT-based radiotherapy in locoregionally-advanced nasopharyngeal cancer. Oncol Lett, 5(3), 889–895. https://doi.org/10.3892/ol.2013.1137

23. Feng, H. X., Guo, S. P., Li, G. R., Zhong, W. H., Chen, L., Huang, L. R., & Qin, H. Y. (2014). Toxicity of concurrent chemoradiotherapy with cetuximab for locoregionally advanced nasopharyngeal carcinoma. Med Oncol, 31(9), 170. https://doi.org/10.1007/s12032-014-0170-x
24. Lee, N., Xia, P., Quivey, J. M., Sultanem, K., Poon, I., Akazawa, C., Akazawa, P., Weinberg, V., & Fu, K. K. (2002). Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: An update of the UCSF experience. Int J Radiat Oncol Biol Phys, 53(1), 12–22. https://doi.org/10.1016/s0360-3016(02)02724-4
25. Niu, X., Hu, C., & Kong, L. (2013). Experience with combination of cetuximab plus intensity-modulated radiotherapy with or without chemotherapy for locoregionally advanced nasopharyngeal carcinoma. J Cancer Res Clin Oncol, 139(6), 1063–1071. https://doi.org/10.1007/s00432-013-1419-z
26. Li, H. M., Li, P., Qian, Y. J., Wu, X., Xie, L., Wang, F., Zhang, H., & Liu, L. (2016). A retrospective paired study: efficacy and toxicity of nimotuzumab versus cisplatin concurrent with radiotherapy in nasopharyngeal carcinoma. BMC Cancer, 16(1), 946. https://doi.org/10.1186/s12885-016-2974-x
27. Zhu, S. Y., Yuan, Y., & Xi, Z. (2012). Radiation recall reaction: Two case studies illustrating an uncommon phenomenon secondary to anti-cancer agents. Cancer Biol Med, 9(3), 202–204. https://doi.org/10.7497/j.issn.2095-3941.2012.03.009
28. Graham, P. H., & Graham, J. L. (2009). Use of deodorants during adjuvant breast radiotherapy: A survey of compliance with standard advice, impact on patients and a literature review on safety. J Med Imaging Radiat Oncol, 53(6), 569–573. https://doi.org/10.1111/j.1754-9485.2009.02125.x
29. Korinko, A., & Yurick, A. (1997). Maintaining skin integrity during radiation therapy. Am J Nurs, 97(2), 40–44.
30. Hassey, K. M., & Rose, C. M. (1982). Altered skin integrity in patients receiving radiation therapy. Oncol Nurs Forum, 9(4), 44–50.
31. Schnur, J. B., Ouellette, S. C., Dilorenzo, T. A., Green, S., & Montgomery, G. H. (2011). A qualitative analysis of acute skin toxicity among breast cancer radiotherapy patients. Psycho-oncology, 20(3), 260–268. https://doi.org/10.1002/pon.1734
32. Wells M. (1998). The hidden experience of radiotherapy to the head and neck: A qualitative study of patients after completion of treatment. J Adv Nurs, 28(4), 840–848. https://doi.org/10.1111/j.1365-2648.1998x.00714.x
33. Wang, R., Wu, F., Lu, H., Wei, B., Feng, G., Li, G., Liu, M., Yan, H., Zhu, J., Zhang, Y., & Hu, K. (2013). Definitive intensity-modulated radiation therapy for nasopharyngeal carcinoma: Long-term outcome of a multicenter prospective study. J Cancer Res Clin Oncol, 139(1), 139–145. https://doi.org/10.1007/s00432-012-1313-0
34. Maduro, J. H., Pras, E., Willemse, P. H., & de Vries, E. G. (2003). Acute and long-term toxicity following radiotherapy alone or in combination with chemotherapy for locally advanced cervical cancer. Cancer Treat Rev, 29(6), 471–488. https://doi.org/10.1016/s0305-7372(03)00117-8
35. Salvo, N., Barnes, E., van Draanen, J., Stacey, E., Mitera, G., Breen, D., Giotis, A., Czarnota, G., Pang, J., & De Angelis, C. (2010). Prophylaxis and management of acute radiation-induced skin reactions: A

systematic review of the literature. Curr Oncol, 17(4), 94–112. https://doi.org/10.3747/co.v17i4.493

36. Ferreira, E. B., Ciol, M. A., Vasques, C. I., Bontempo, P., Vieira, N. N., Silva, L. F., Avelino, S. R., Dos Santos, M. A., & Dos Reis, P. E. (2016). Gel of chamomile vs. urea cream to prevent acute radiation dermatitis in patients with head and neck cancer: A randomized controlled trial. J Adv Nurs, 72(8), 1926–1934. https://doi.org/10.1111/jan.12955
37. Menêses, A. G., Reis, P., Guerra, E., Canto, G. L., & Ferreira, E. B. (2018). Use of trolamine to prevent and treat acute radiation dermatitis: A systematic review and meta-analysis. Rev Lat Am Enfermagem, 26, e2929. https://doi.org/10.1590/1518-8345.2035.2929
38. Censabella S, Claes S, Orlandini M, Braekers R,Thijs H,&Bulens P. (2014). Retrospective study of radiotherapy-induced skin reactions in breast cancer patients: reduced incidence of moist desquamation with a hydroactive colloid gel versus dexpanthenol. Eur J Oncol Nurs,18(5):499-504. https://doi.org/10.1016/j.ejon.2014.04.009
39. Ferreira, E. B., Vasques, C. I., Gadia, R., Chan, R. J., Guerra, E. N., Mezzomo, L. A., De Luca Canto, G., & Dos Reis, P. E. (2017). Topical interventions to prevent acute radiation dermatitis in head and neck cancer patients: A systematic review. Support Care Cancer, 25(3), 1001–1011. https://doi.org/10.1007/s00520-016-3521-7

# Tables

Due to technical limitations, tables PDF is only available as a download in the Supplemental Files section.

# Figures

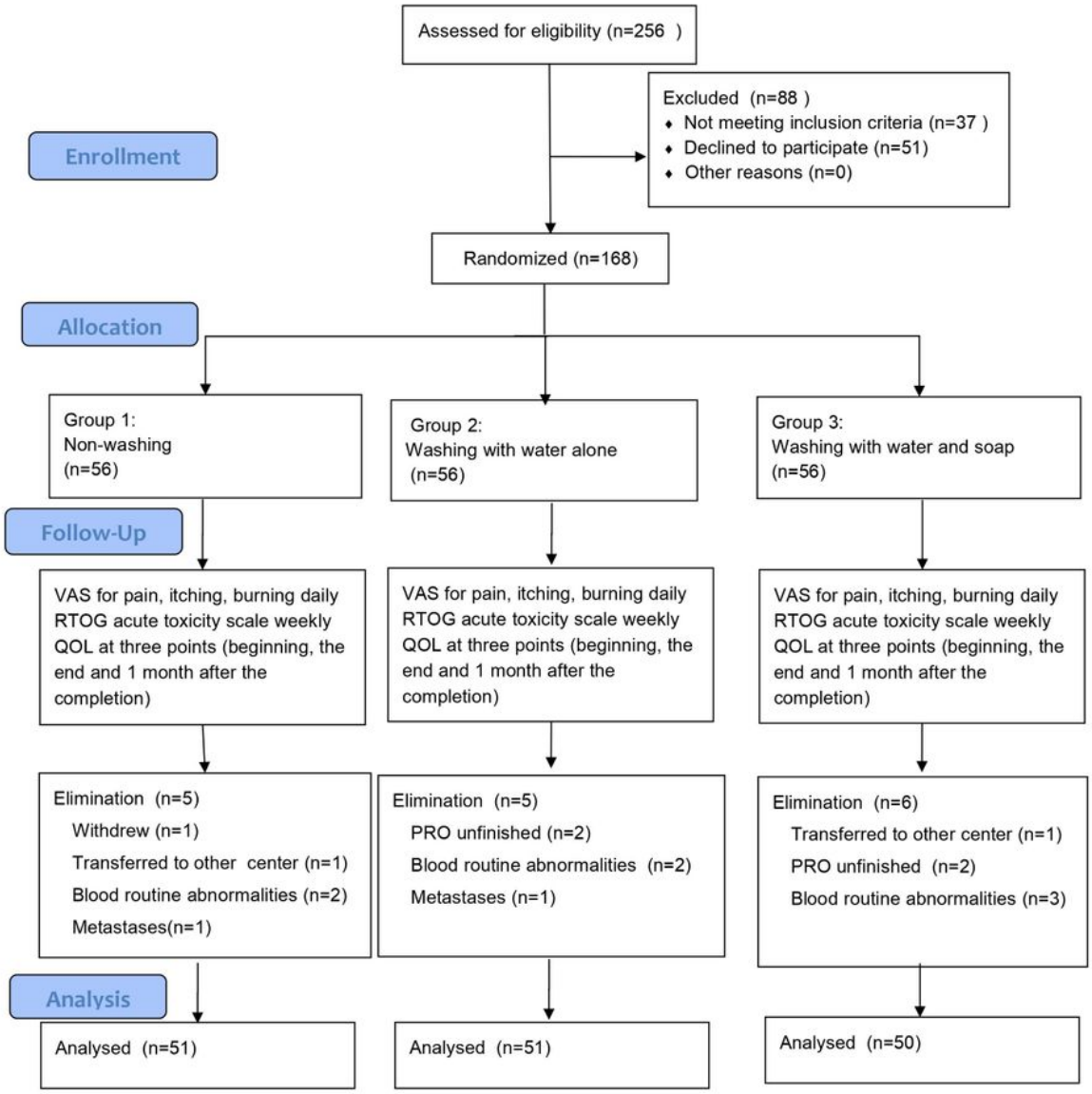


**Figure 1**

Participations enrolment and data collection process

# Supplementary Files

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