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RESEARCH ARTICLE

Comparative effects of early versus delayed fat grafting following radiation exposure in rats

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Abstract

Background: Autologous fat grafting has emerged as a promising technique to mitigate radiation-induced tissue damage during breast reconstruction. This study aimed to evaluate the effects of fat grafting timing on the irradiated skin in a rat model.

Materials and Methods: Twenty female Wistar albino rats were divided into two groups: early grafting (EG) and delayed grafting (DG). All the rats received 20-Gy external beam irradiation of the anterior thoracic wall. In the EG group, fat grafting was performed one day post-irradiation, whereas in the DG group, it was performed 21 ds should be days. The contralateral side of each rat served as a control and received saline injection. Macroscopic evaluation of the skin quality and necrosis rates, microangiography, and histological analyses were performed.

Results: Results showed that necrosis rates were significantly lower in grafted tissues than in control sites in both the EG and DG groups. Although the EG exhibited less fibrosis and higher vascularization, the differences were not statistically significant. Histological assessments revealed reduced inflammatory cell infiltration and better preservation of skin appendages in the grafted areas, particularly in the EG. Microangiography confirmed adequate neovascularization around the graft.

Conclusion: Despite the limitations in sample size and grafting intervals, this study suggests that fat grafting, regardless of timing, can improve tissue integrity and vascularization in irradiated skin. Further research is needed to optimize protocols and enhance patient outcomes in breast reconstruction following radiotherapy.

Keywords: fat grafting, irradiated skin, breast reconstruction, radiotherapy, neovascularization, tissue integrity.

Introduction

Autologous fat transfer (AFT) has gained significant popularity in plastic surgery for both reconstruction and cosmetic purposes. In 2009, the American Society of Plastic Surgeons Task Force on Autologous Fat Grafting (AFG) deemed it a safe procedure with low complication rates, leading to its widespread adoption [1]. Its applications range from soft-tissue augmentation of breasts, buttocks, hips, face, and hands to reconstructive uses such as breast reconstruction contour problems and correction of various deformities [1].

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Radiotherapy plays a crucial role in reducing locoregional recurrence and improving the overall survival of patients with breast cancer. Studies have shown that postoperative radiotherapy (PORT) decreases locoregional failure rates in high-risk breast cancer patients following modified radical mastectomy [2,3]. For patients with triple-negative breast cancer, radiotherapy has been associated with a significantly higher 3-year actuarial locoregional relapse-free survival probability than those who did not receive radiation (79.6% vs. 57.9%, P = 0.049) [4]. However, the combination of breast reconstruction and radiotherapy presents a challenge to plastic surgeons. Radiation can potentially affect the viability of reconstructed tissues and cosmetic outcomes.

Plastic surgeons have subsequently translated this insight into the clinical practice. Typically, clinical fat graft procedures are performed once the lasting effects of radiotherapy become apparent. Is there a link between the beneficial effect of a fat graft on the irradiated area and the timing of its application? Can the adverse effects of radiotherapy be mitigated by administering fat grafts to the irradiated area during the acute phase? These questions formed the basis of our hypotheses. This study aimed to evaluate whether controlled fat grafting on irradiated tissue enhances skin quality through macroscopic, histologic, and microangiographic objective data, while also examining how the timing of fat grafting influences the outcome.

Materials And Methods

Study design and ethical approval

This study was prospectively designed and conducted in accordance with protocols approved by the Hacettepe University Animal Experiments Local Ethics Committee (approval no. 2014/33-05). The experimental protocol adhered to the guidelines outlined in the “Guide for the Care and Use of Laboratory Animals”. A total of 20 non-immunosuppressed female Wistar albino rats were used, with four animals specifically allocated for microangiography.

Radiation dose optimization

To ascertain the appropriate radiation dose for the study, preliminary experiments were conducted involving two groups of rats, each receiving either a low dose (20 Gy, n=2) or a high dose (35 Gy, n=2) of irradiation. After a period of six weeks, both groups demonstrated macroscopic and histological signs of radiation-induced damage (Figure 1). Following a collaborative evaluation by specialists in radiation oncology and histopathology, a 20 Gy dose was selected for the main study. This dose was considered adequate to elicit a measurable fibrotic response without inducing excessive tissue damage, which could potentially confound the results [5]. A dose threshold of 30-35 Gy has been associated with an increased likelihood of fibrosis [6]. Consequently, a dose of 20 Gy was selected.

Animal model and surgical procedures

Female Wistar albino rats weighing 250-400 g (obtained from the Hacettepe University Animal Research Center) were housed under specific pathogen-free conditions. Environmental controls were maintained at a temperature of 22 ± 2°C, relative humidity of 55 ± 10%, and a 12-hour light/dark cycle. The animals had ad libitum access to standard rodent chow and filtered tap water.

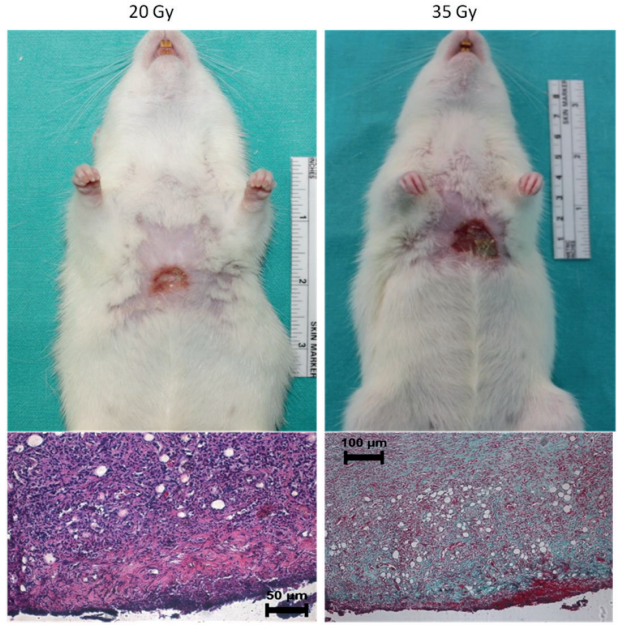

Figure 1. Macroscopic and histological presentation of radiation-induced tissue damage following exposure to 20 Gy and 35 Gy. Observed effects include dermal thickening, erythema, alopecia, and ulceration in both dose groups

The surgical procedures were performed under aseptic conditions. General anesthesia was induced via intraperitoneal injection of a mixture of ketamine hydrochloride (87.5 mg/kg; Ketalar, Pfizer) and xylazine (12.5 mg/kg; Rompun, Bayer). The surgical site was prepared by shaving the anterior thoracic wall and disinfecting it with 10% povidone-iodine solution. Fat grafts were harvested from the inguinal fat pads. The fat tissue was then processed according to the technique described by Piasecki et al., involving gentle washing with sterile saline and careful removal of any connective tissue or blood clots [7]. Fat grafts were harvested from the inguinal fat pads under aseptic conditions. The harvested adipose tissue was processed by gentle washing with sterile saline and manual removal of visible blood clots and connective tissue remnants, following a conventional purification approach. No enzymatic digestion, chemical dissociation, centrifugation-based stromal isolation, or mechanical emulsification/filtration technique was applied. Thus, the grafted material represented structurally preserved whole adipose tissue rather than microfat or nanofat. The harvested fat grafts were approximately 0.5 cm^3 in volume.

The animals were divided into two experimental groups (n=8 per group) based on the timing of fat grafting.

- Early Grafting (EG): Fat grafting was performed on the left breast one day after the completion of radiotherapy. The right breast received a sham injection of an equivalent volume of sterile saline (0.5 mL) as an Early Control (EG-C).
- Delayed Grafting (DG): Fat grafting was performed on the left breast 21 days after radiotherapy. The right breast received a sham injection of sterile saline (0.5 mL) as the Delayed Control (DG-C).

This paired study design, in which each animal served as its own control, was implemented to reduce inter-animal variability and enhance the statistical power of the comparative assessment.

Irradiation protocol

Based on the pilot study, the animals were positioned in a supine position to facilitate consistent irradiation of a defined 4 × 6-cm2 area on the anterior thoracic wall. The animals received a single fraction of 20-Gy external beam irradiation using a Chinac DHX Sn3810 linear accelerator. The irradiation parameters were as follows: beam energy, 4 MeV; dose rate, 1000 cGy/min; and source-to-skin distance, 100 cm from the top of a 0.5 cm thick bolus material placed on the skin surface. Lead blocks of 5 mm thickness were carefully positioned to shield the rats' vital organs (lungs, heart, and abdominal organs) from the direct effects of irradiation, minimizing off-target radiation exposure.

Assessment of skin quality and tissue viability

Standardized digital photographs were acquired 11 weeks post-irradiation using a Canon EOS 70D camera with a macro-lens. The camera was mounted on a tripod to maintain consistent distance and angle perpendicular to the skin flap. Consistent lighting conditions were ensured using a calibrated LED light source. Serial photography of the skin surface was performed to visually assess the macroscopic evidence of irradiation-induced changes, including erythema, ulceration, and fibrosis. The acquired images were transferred to a computer, and the areas exhibiting tissue necrosis, as well as the total skin flap areas, were quantified in pixels using ImageJ Software (version1.48v; Java). Two independent investigators, blinded to the treatment groups, performed image analysis.

Microangiography

To evaluate the microcirculation within the grafted fat flaps, microangiography was performed on a subset of animals (n=2 from each experimental group). The procedure involved systemic infusion of lead oxide and gelatin contrast agent to visualize the microvasculature [8].

Animals were anesthetized as described previously. Midline laparotomy was performed to expose the abdominal aorta. A 24-gauge catheter was inserted into the abdominal aorta and the lead oxide/gelatin mixture was infused at a controlled rate. The contrast solution was prepared by mixing lead oxide powder with 5% gelatin solution in sterile water at a ratio of 1:2 (w/v). The mixture was heated gently to dissolve the gelatin and create a homogeneous suspension. The solution was infused at a rate of approximately 1 mL/min, with a total volume of 25 mL per animal, to ensure complete opacification of the microvasculature within the fat flaps. The infusion was continued until the contrast agent visibly replaced the blood in the venous outflow, indicating an adequate filling of the microvascular network.

Following infusion, the fat flaps were carefully dissected and harvested to ensure minimal microvasculature disruption. The harvested flaps were then stored at 4°C for 24 hours to allow gelatin to solidify, thereby preserving the vascular architecture. Subsequently, all flaps were subjected to radiography by using a soft X-ray machine. Radiographic imaging parameters were set at 25 kV and 10 mA, consistent with previously established protocols for microangiography [9]. Images were acquired using a high-resolution digital detector.

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 19.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, Illinois USA,). The Kolmogorov-Smirnov test was used to assess the distribution patterns of the quantitative data. Descriptive statistics are presented as mean ± standard deviation. Histological scores, including neovascularization and acute inflammation, as well as macroscopic evaluations, specifically the percentage of skin flap survival, were analyzed using the nonparametric Kruskal-Wallis test. Multiple comparisons were performed using the Dunn and Fisher-Freeman-Holton tests. A p-value of less than 0.05 was considered indicative of statistical significance.

Results

Macroscopic evaluation of skin quality and tissue necrosis

By the end of the eleventh week after irradiation, a comprehensive topographical evaluation was conducted across all groups to assess skin quality and detect necrotic regions. The total necrosis rates were quantified as follows: 1.65%, 6.86%, 2.57%, and 7.08% in the EG, EG-C, DG, and DG-C groups, respectively (Figure 2). Statistical analysis revealed that the necrotic areas in the grafted sites were significantly smaller than those on their respective control sides (p=0.012 and p=0.025, respectively). Despite the lower necrosis ratio in the EG, the difference between the two groups was not statistically significant (p=0.574). Figure 2 provides a detailed summary of the macroscopic evaluation.

Microangiography

Microangiography was performed in a subset of four animals (two from each experimental group) to assess vascularization within the grafted areas. Angiographic results were consistent with macroscopic observations, showing adequate vascular networks in both early and delayed grafts. No gross differences in vascular patterns were observed between the two groups (Figure 3).

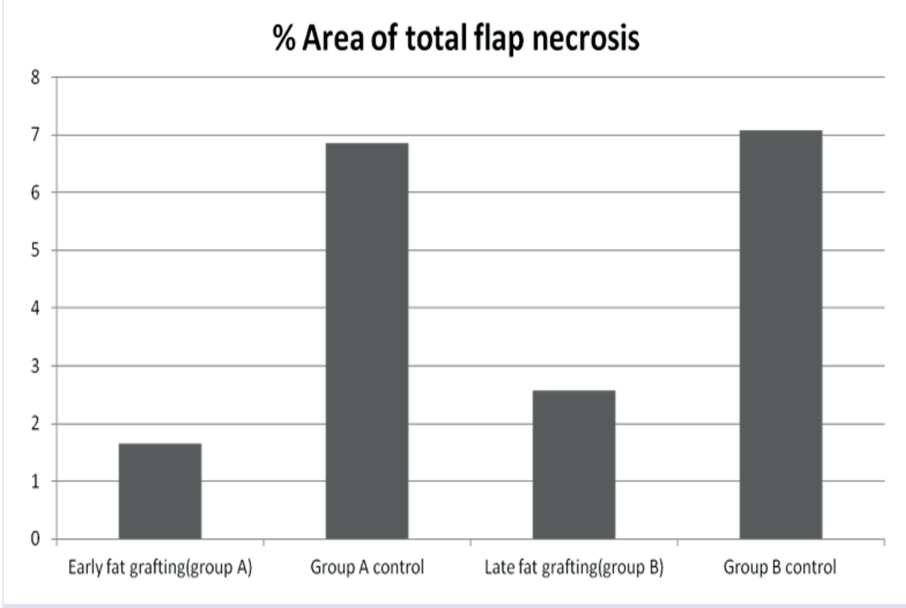

Figure 2. Quantification of necrotic areas at week 11 post-irradiation

Histological analysis

Histopathological examination revealed similar tissue responses in both the graft groups. The overall skin structure was preserved, and skin appendages such as sweat glands and hair follicles appeared largely intact. Fat grafts were localized within the dense and irregular connective tissue layer between the epidermis and dermis and were often surrounded by a capsule of fibrous tissue. Although some fibrotic changes were noted within the grafts, they demonstrated sufficient vascularization, with evidence of neovascular formation.

In both the EG and DG groups, dermal cell infiltration was markedly reduced compared with their respective control groups (Figure 4).

Nevertheless, focal disruptions in tissue integrity, fibrosis in the deep dermis, and areas of muscle fiber necrosis were also observed (Figure 5). Collagen bundles were disrupted by interstitial edema in several regions.

Dermal fibrosis grading indicated that 87.5% of the animals in the EG group had mild fibrosis compared to 62.5% in the DG group. In the control group, mild fibrosis was observed in 62.8% of the EG-C animals and in 25.0% of the DG-C animals. Although the EG group exhibited less fibrosis than the DG group, a statistical comparison was not feasible owing to the limited sample size (Figure 6).

Quantitative histological measures showed no significant differences between the groups. The average number of blood vessels surrounding fat grafts was 3.8 in the EG group and 3.0 in the DG group (p=0.345). The average infiltrative cell counts were 12.8 cells per field in the EG group and 15.3 in the DG group (p=0.705). Comparisons with the control groups indicated a trend toward decreased infiltration in grafted tissues; however, these differences were not statistically significant (p=0.068 for the EG vs. EG-C group, p=0.080 for the DG vs. DG-C group).

Epidermal thickness measurements revealed no statistically significant differences among the groups: 76.90 µm in EG, 112.50 µm in DG, 83.01 µm in EG-C, and 77.24 µm in DG-C (p=0.161). Similarly, no significant difference was observed between the control sides of the EG and DG groups (p=0.651 and p=0.149, respectively) (Figure 7).

Dermal thickness was measured as 869.91 µm in EG, 904.65 µm in DG, 864.47 µm in EG-C, and 741.17 µm in

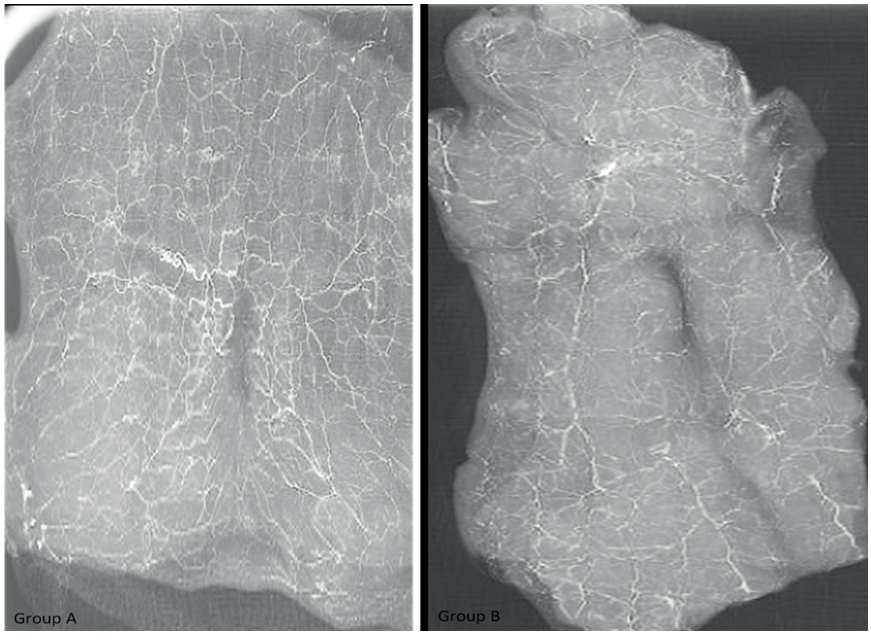

Figure 3. Representative microangiographic images from each experimental group, illustrating the microvascular architecture

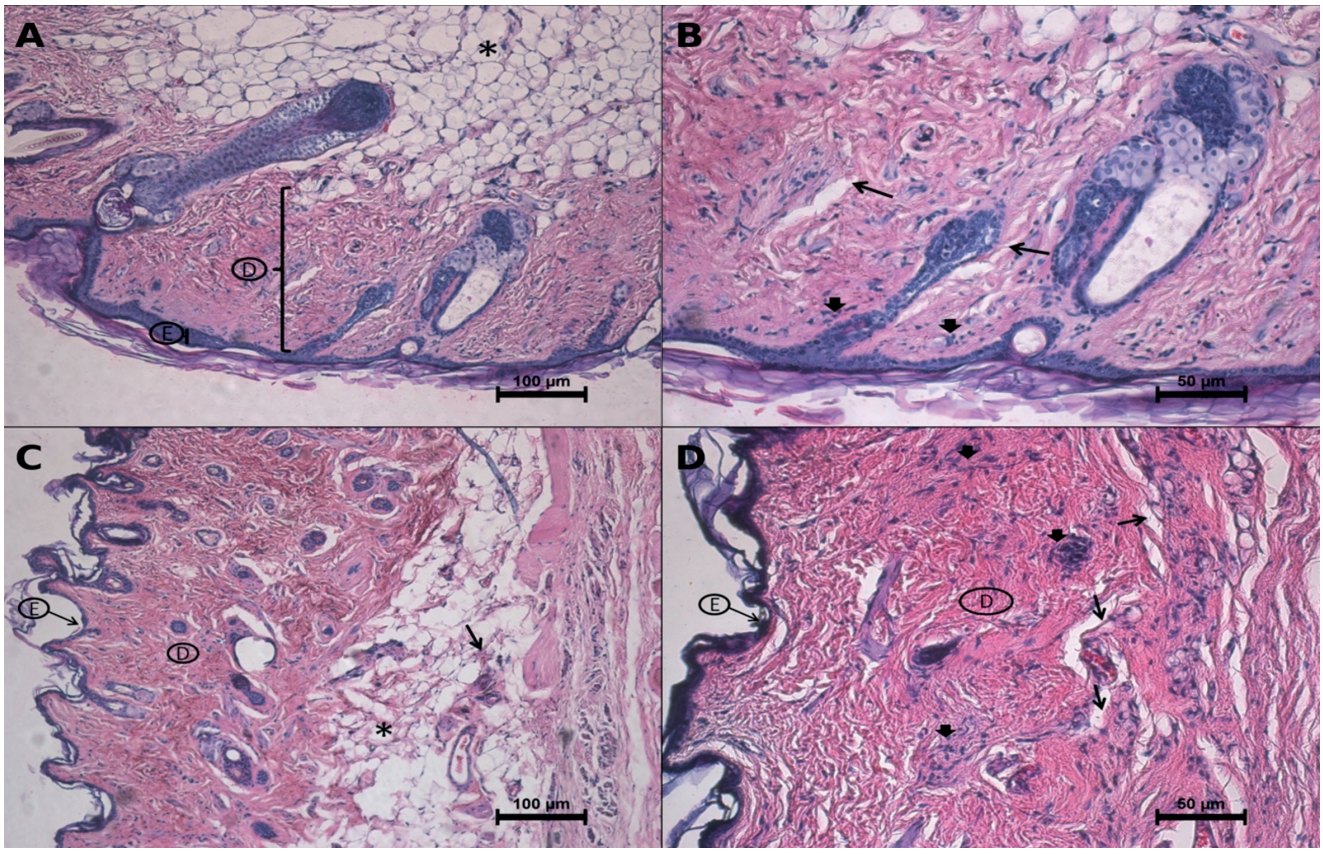

Figure 4. Histological evaluation of skin grafts in early and late fat graft groups

(A) Early fat graft group exhibiting a thin, continuous epidermis (E) and dermis (D) with underlying fat graft (magnification ×100). (B) Early fat graft group demonstrating cellular infiltration in the dermis (thick arrow) and collagen fiber separation due to edema (thin arrow; magnification ×200). (C) Late fat graft group with a thin, continuous epidermis (E) and dermis (D) overlying the fat graft, and a necrotic area within the fat graft (arrow; magnification ×100). (D) Late fat graft group showing cellular infiltration in the dermis (thick arrow) and collagen fiber separation due to edema (thin arrow; magnification ×200).

DG-C. These differences were not statistically significant across the groups (EG vs. DG, p=0.705; EG-C vs. DG-C, p=0.956 and p=0.103) (Figure 8).

Discussion

In this experimental study, the macroscopic, angiographic, and histopathological findings collectively suggest that autologous fat grafting, whether applied immediately or with delay following irradiation, exerts beneficial effects on tissue integrity and vascularization in the irradiated skin. Macroscopic evaluation revealed that necrosis rates were lower in the grafted tissues than in the control sites, with statistically significant differences observed in both the early and delayed intervention groups. Although EG resulted in less fibrosis and greater vascularization than DG, these differences were not statistically significant. Histological assessments further demonstrated reduced inflammatory cell infiltration and better preservation of skin appendages in the grafted areas, particularly in the early intervention group. Microangiographic findings supported these observations, showing no overt difference between early and delayed grafts but confirming adequate neovascularization around the grafts. Overall, while sample size limitations restricted the statistical power for some comparisons, the cumulative data support the notion that fat grafting mitigates radiation-induced tissue damage, with early application potentially offering modest advantages.

Fat grafting has demonstrated promising potential in mitigating radiation-induced tissue damage. Research has shown that fat grafts enriched with adipose-derived stromal cells (ASCs) can significantly enhance

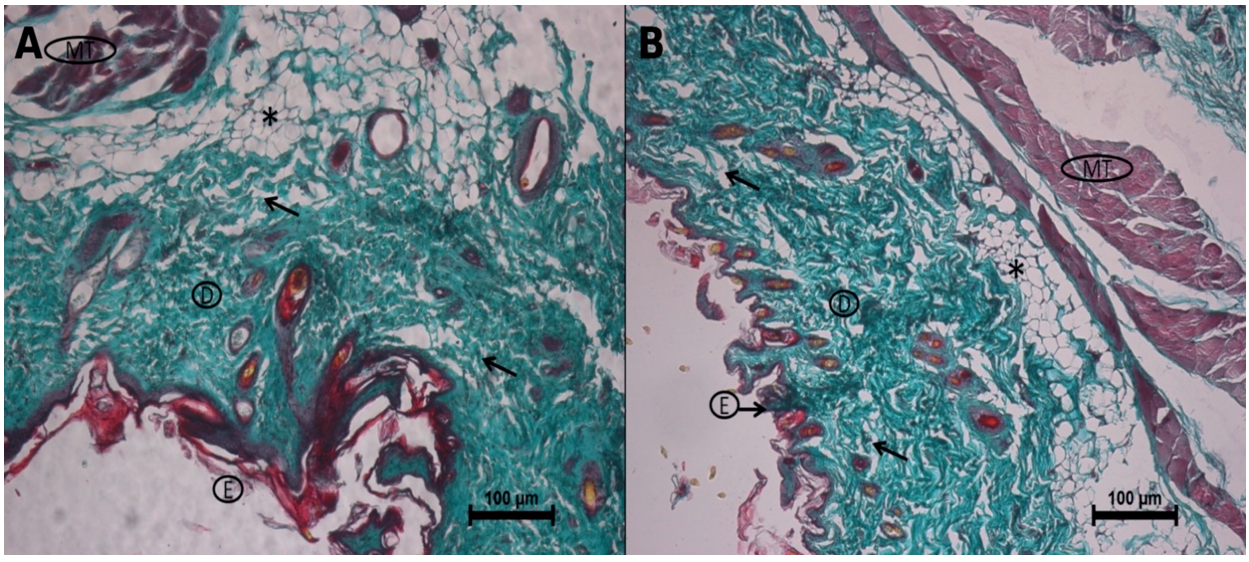

Figure 5. Histological analysis of skin grafts using Masson Trichrome staining in early and late fat graft groups (magnification ×100)

(A) Early fat graft group exhibiting a thin, continuous epidermis (E) and dermis (D) with collagen fiber separation due to edema (arrow), an underlying fat graft, and separated muscle fibers due to edema (MT: arrow). (B) Late fat graft group with a thin, continuous epidermis (E) and dermis (D), collagen fiber separation due to edema (arrow), an underlying fat graft, and separated muscle fibers due to edema (MT: arrow).

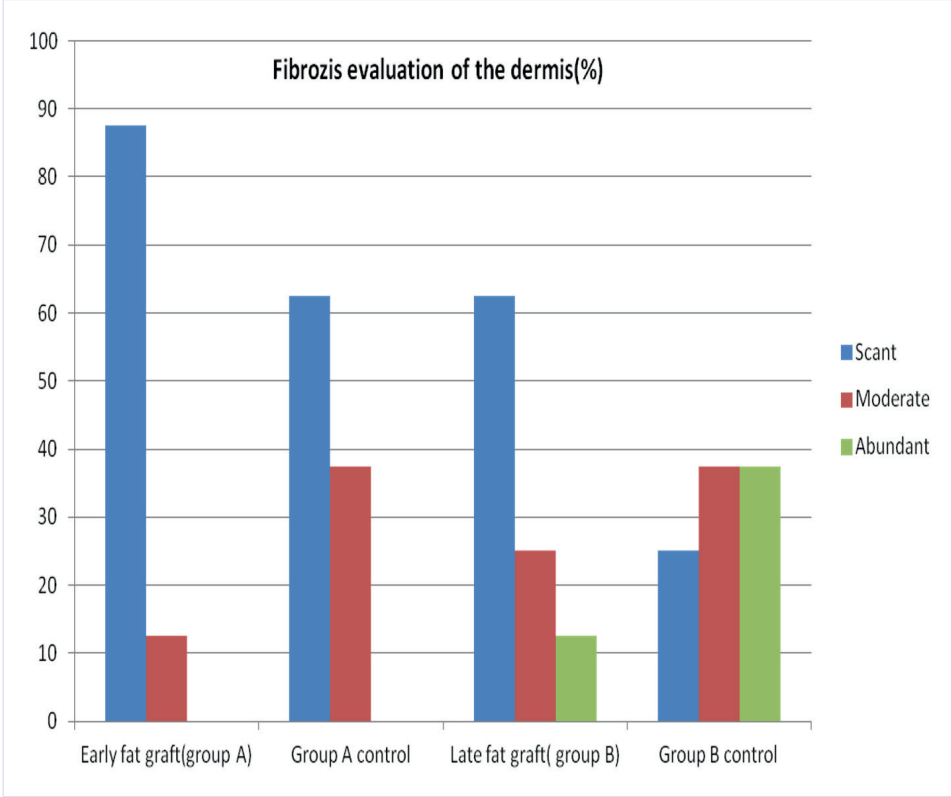

Figure 6. Quantitative assessment of dermal fibrosis

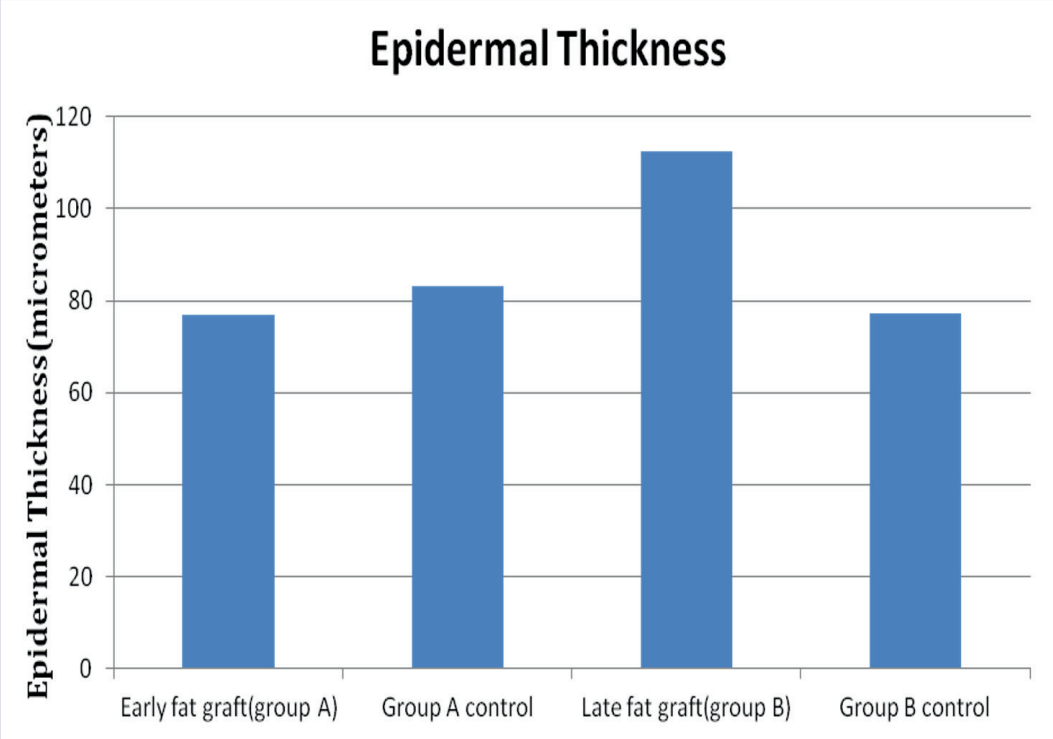

Figure 7. Epidermal thickness (μm) in EG, DG, EG-C, and DG-C groups

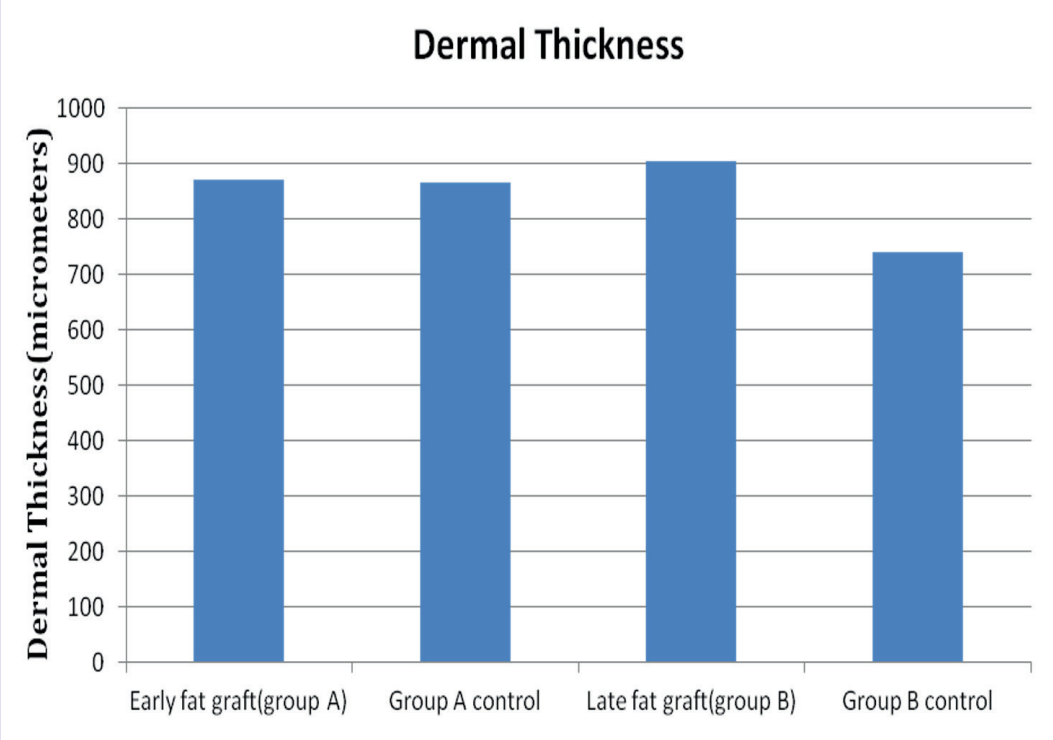

Figure 8. Dermal thickness (μm) in EG, DG, EG-C, and DG-C groups

the outcomes of treating radiation-induced fibrosis [10]. The antifibrotic effects of ASCs, especially the CD74-positive subpopulation, have been observed to reduce skin stiffness, dermal thickness, and collagen content in irradiated areas [10]. These CD74+ ASCs show increased expression of growth factors such as hepatocyte growth factor, fibroblast growth factor 2, and transforming growth factor β3, while reducing the levels of pro-fibrotic TGF-β1 [10]. The mechanisms by which fat grafts reduce radiation damage involve intricate tissue-remodeling processes. Although many adipocytes in the graft initially die, they are replaced by adipogenesis, with new adipocytes emerging as early as one week post-grafting [11]. This regeneration is facilitated by the angiogenic properties of ASCs, which provide various growth factors that enhance graft vascularization [12]. The gradual absorption of lipid droplets from dead adipocytes also helps maintain space for adipocyte regeneration [11]. The ability of fat grafting to reduce radiation damage likely stems from a combination of factors, including the antifibrotic properties of specific ASC subpopulations, promotion of angiogenesis, and support of tissue regeneration through dynamic remodeling processes. These findings suggest that optimized fat grafting techniques could play a crucial role in addressing radiation-induced tissue damage in reconstructive and aesthetic surgeries. In this preclinical study, we investigated the effect of fat grafting timing on irradiated skin tissue by comparing early and delayed applications in a controlled rat model. Our findings demonstrate that fat grafting, regardless of timing, improves tissue quality by reducing necrosis and enhancing vascularization, with a slight trend favoring early intervention. These results support the hypothesis that fat grafting may mitigate radiation-induced soft-tissue damage when applied in proximity to irradiation.

Literature supports the necrosis-reducing effect of fat grafting in the early post-radiotherapy period. AFT is a procedure used to repair adipose tissue following trauma, burns, tumor resection, and lipodystrophy [13]. However, the issue of low graft permanence persisted. The underlying causes are not fully understood and may involve damage to mature adipocytes or mesenchymal progenitor cells (ASC) as well as apoptosis and involution post-transplantation [13]. While adipose tissue-conditioned medium has been shown to inhibit fibroblast differentiation into myofibroblasts, ASC or lipid-conditioned medium do not exhibit this effect [14]. This highlights the significance of whole adipose tissue in fat grafting. Additionally, radiotherapy induces an inflammatory response in adipose tissue and elevates autotaxin secretion [15]. This underscores the potential advantages of fat grafting radiotherapy. In our study, consistent with previous research, macroscopic and histological analyses demonstrated that fat-grafted areas showed reduced necrosis and fibrotic remodeling compared to control sites. Although not statistically significant, the early graft group consistently exhibited lower fibrosis scores and higher vessel densities. These findings imply that the regenerative effect of fat grafts may partly rely on early neovascularization and the modulation of local inflammation. In conclusion, literature supports the necrosis-reducing effect of fat grafts in the early post-radiotherapy period. ASC-enriched AFT has been shown to decrease early cell death and enhance vasculogenesis [13]. These findings support the use of fat grafting in scar treatment and suggest that it may be a viable option for tissue repair following radiotherapy.

No direct information is available regarding comparisons between early and delayed fat grafting radiotherapy. However, several key points regarding fat grafting are noteworthy in this context: fat grafting is a widely employed technique in breast reconstruction and may help reduce complications following radiotherapy. When combined with a latissimus dorsi flap, fat grafting can increase breast volume in a single surgery [16]. Additionally, fat grafting can be used to mitigate radiation damage [1]. However, there are various approaches to determine the timing of fat grafting. Some studies have performed fat grafting as a secondary surgery a month after the flap procedure [16], while others recommend combining it with the same procedure. Nonetheless, there is no definitive consensus regarding the optimal timing of RT. The timing of fat grafting in irradiated tissue remains a contentious issue in the literature, with some studies suggesting enhanced efficacy with delayed grafting, whereas others advocate for early intervention. Our findings contribute to this debate by suggesting that immediate grafting may yield comparable, if not superior, histological outcomes. Notably, our model offers early phase biological insights that are distinct from clinical reconstruction timelines.

From a translational perspective, the grafted material used in the present study most closely corresponds to conventionally processed whole adipose tissue rather than microfat or nanofat. This distinction is relevant because macrofat and microfat are mainly used for volume restoration and contour correction, whereas

nanofat is generally preferred for regenerative purposes such as improving skin quality, scar remodeling, and wound healing [17]. However, robust comparative clinical data directly evaluating the success rates of these different graft types remain limited [18]. Another important issue is oncologic safety. Although current clinical evidence has not demonstrated a clear increase in locoregional recurrence after autologous fat grafting in breast reconstruction, the biological activity of adipose-derived stromal/stem cell–containing grafts still warrants caution[19]. Therefore, while the regenerative effects of fat grafting in irradiated tissue are promising, their application in oncologic reconstruction should be interpreted carefully, with particular attention to long-term surveillance.

Despite these encouraging findings, this study has several important limitations that should be acknowledged. The relatively small sample size (n=8 per group) limited the statistical power, particularly for comparisons with borderline significance. Although increasing the number of experimental animals was not feasible owing to ethical and logistical constraints inherent to in vivo radiation studies, the use of internal controls comparing grafted and control sites within the same animal helped mitigate inter-subject variability and partially compensated for this limitation. Nonetheless, results involving marginal p-values should be interpreted with caution. Additionally, only two discrete grafting time points were examined, which may not fully capture the dynamic trajectory of radiation-induced inflammation and tissue remodeling. The microangiographic analysis was restricted to a small subset of animals (n=4), limiting the robustness of the vascularization data. Furthermore, the lack of molecular or immunohistochemical analyses prevents deeper insight into the underlying mechanisms. Another limitation of this study is that late radiologic consequences of fat grafting could not be evaluated in this experimental model. In clinical practice, long-term fat grafting may lead to fat necrosis, oil cysts, and calcifications or microcalcifications, which may occasionally be misinterpreted as malignancy on breast imaging. Even though most of these findings are benign, they can complicate postoperative assessment and may necessitate additional diagnostic procedures. Therefore, future clinical studies should incorporate long-term radiologic surveillance. Future studies should include intermediate grafting intervals, larger sample sizes, and advanced tissue characterization techniques to better elucidate the biological effects of fat grafting in irradiated tissues.

Conclusion

In conclusion, this study provides valuable insights into the potential benefits of autologous fat grafting in mitigating radiation-induced tissue damage in breast reconstruction. These findings suggest that fat grafting, whether applied immediately or with delay following irradiation, can improve tissue integrity and vascularization in the irradiated skin. Macroscopic and histological assessments demonstrated reduced necrosis rates, decreased inflammatory cell infiltration, and better preservation of skin appendages in grafted areas than in control sites. Although early grafting showed a trend towards less fibrosis and greater vascularization, the differences were not statistically significant. These results contribute to the ongoing debate regarding the optimal timing of fat grafting post-radiotherapy and highlight the need for further research with larger sample sizes and more diverse grafting intervals. Despite these limitations, this study underscores the potential of fat grafting as a valuable technique in breast reconstruction following radiotherapy, warranting continued investigation to refine the protocols and improve patient outcomes.

Author contributions

Conception and design: I.U.O., E.R.H., G.Y., A.K.; Data acquisition: I.U.O., A.K.; Data analysis: I.U.O., O.E., E.K., P.A., G.Y., A.K.; Data interpretation: I.U.O., O.E., P.A., E.R.H., A.K.; Drafting of the manuscript: I.U.O., O.E., E.K., E.R.H., G.Y., A.K.; Critical revision of the manuscript: I.U.O., O.E., P.A. All authors reviewed the results, approved the final version of the manuscript, and agreed to be accountable for all aspects of this study.

Ethical approval

This study was approved by the Hacettepe University Animal Experiments Local Ethics Committee (Date: June 13, 2014, Decision/Protocol No: 2014/33-05). Informed consent was not required for this study.

Data availability statement

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

Conflict of interest

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The authors declare that this study received no funding.

Generative AI statement

The authors declare that no generative AI or AI-assisted technologies were used in the writing or preparation of this study.

References

[1] Landau MJ, Birnbaum ZE, Kurtz LG, Aronowitz JA. Review: proposed methods to improve the survival of adipose tissue in autologous fat grafting. Plast Reconstr Surg Glob Open 2018;6(8):e1870. **[Crossref]**

[2] Hunt KK, Baldwin BJ, Strom EA, et al. Feasibility of postmastectomy radiation therapy after TRAM flap breast reconstruction. Ann Surg Oncol 1997;4(5):377-84. **[Crossref]**

[3] Kolářová I, Melichar B, Sirák I, et al. The Role of Adjuvant Radiotherapy in the Treatment of Breast Cancer. Curr Oncol 2024;31(3):1207-20. **[Crossref]**

[4] Dragun AE, Pan J, Rai SN, Kruse B, Jain D. Locoregional recurrence in patients with triple-negative breast cancer: preliminary results of a single institution study. Am J Clin Oncol 2011;34(3):231-7. **[Crossref]**

[5] Straub JM, New J, Hamilton CD, Lominska C, Shnayder Y, Thomas SM. Radiation-induced fibrosis: mechanisms and implications for therapy. J Cancer Res Clin Oncol 2015;141(11):1985-94. **[Crossref]**

[6] Rosen II, Fischer TA, Antolak JA, et al. Correlation between lung fibrosis and radiation therapy dose after concurrent radiation therapy and chemotherapy for limited small cell lung cancer. Radiology 2001;221(3):614-22. **[Crossref]**

[7] Piasecki JH, Gutowski KA, Lahvis GP, Moreno KI. An experimental model for improving fat graft viability and purity. Plast Reconstr Surg 2007;119(5):1571-83. **[Crossref]**

[8] Banic A, Nilsson U, Francis I. Magnification angiography and histology for the evaluation of microvascular anastomosis. Microsurgery 1990;11(2):102-7. **[Crossref]**

[9] Nacak U, Calis M, Atilla P, Cetin A, Aksu AE. Extracorporal shock wave therapy as a delay procedure to improve viability of zone 4: an experimental study in a rat TRAM flap model. Ann Plast Surg 2016;77(2):e15-20. **[Crossref]**

[10] Borrelli MR, Patel RA, Adem S, et al. The antifibrotic adipose-derived stromal cell: grafted fat enriched with CD74+ adipose-derived stromal cells reduces chronic radiation-induced skin fibrosis. Stem Cells Transl Med 2020;9(11):1401-13. **[Crossref]**

[11] Kato H, Mineda K, Eto H, et al. Degeneration, regeneration, and cicatrization after fat grafting: dynamic total tissue remodeling during the first 3 months. Plast Reconstr Surg 2014;133(3):303e-313e. **[Crossref]**

[12] Garza RM, Rennert RC, Paik KJ, et al. Studies in fat grafting: part IV. Adipose-derived stromal cell gene expression in cell-assisted lipotransfer. Plast Reconstr Surg 2015;135(4):1045-55. **[Crossref]**

[13] Piccinno MS, Veronesi E, Loschi P, et al. Adipose stromal/stem cells assist fat transplantation reducing necrosis and increasing graft performance. Apoptosis 2013;18(10):1274-89. **[Crossref]**

[14] Higginbotham S, Workman VL, Giblin AV, Green NH, Lambert DW, Hearnden V. Inhibition and reversal of a TGF-β1 induced myofibroblast phenotype by adipose tissue-derived paracrine factors. Stem Cell Res Ther 2024;15(1):166. **[Crossref]**

[15] Meng G, Tang X, Yang Z, et al. Implications for breast cancer treatment from increased autotaxin production in adipose tissue after radiotherapy. FASEB J 2017;31(9):4064-77. **[Crossref]**

[16] Niddam J, Vidal L, Hersant B, Meningaud JP. Primary fat grafting to the pectoralis muscle during latissimus dorsi breast reconstruction. Plast Reconstr Surg Glob Open 2016;4(11):e1059. **[Crossref]**

[17] Grünherz L, Sanchez-Macedo N, Florian SF, Michelle M, Nicole L. Nanofat applications: from clinical esthetics to regenerative research: potential applications of nanofat in tissue regeneration with a focus on wound healing and vascularization. Curr Opin Biomed Eng 2019;10:174-80.

[18] La Padula S, Ponzo M, Lombardi M, et al. Nanofat in Plastic reconstructive, regenerative, and aesthetic surgery: a review of advancements in face-focused applications. J Clin Med 2023;12(13):4351. **[Crossref]**

[19] Lo Torto F, Patanè L, Abbaticchio D, Pagnotta A, Ribuffo D. Autologous fat grafting (afg): a systematic review to evaluate oncological safety in breast cancer patients. J Clin Med 2024;13(15):4369. **[Crossref]**