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MRI Analysis of Chronological Changes in Free-flap Volume in Head and Neck Reconstruction by Volumetry

Yuki SAKAMOTO[*1], Taro TAKAHARA[*2], Yoshihide OTA[*1], Takayuki AOKI[*1], Hiroshi YAMAZAKI[*1], Mitsunobu OTSURU[*1], Miho TAKAHASHI[*1], Ken-ichi AOYAMA[*1], Akihiro KANEKO[*1], Shunichi KAWADA[*3], Tamaki ICHIKAWA[*3], Kotaro IMAGAWA[*4] and Muneo MIYASAKA[*4]

*Department of [*1]Oral and Maxillofacial surgery, [*3]Radiology, [*4]Plastic surgery Tokai University School of Medicine*
*Department of [*2] Biomedical Engineering, Tokai University School of Engineering*

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Objective: To evaluate changes in flap volumes for head and neck cancer patients by MRI.
Methods: MRI examinations of a total of 21 head and neck cancer patients (13 males and 8 females; average age, 67 years) were performed after surgery to monitor changes in flap volumes, including muscle and fat content, using volumetric analysis of T2-weighted images at 1, 3, 6, and 12 months after surgery.
Results: Fat-to-muscle ratios of all flaps at 1 month varied (muscle/fat ratio, 0.04–0.96). Flap volumes in all patients decreased at 12 months after surgery. The average final volumes of overall, muscle, and fat volumes reached 76.9% ± 5.2%, 37.1% ± 3.7%, and 85.5% ± 5.7%, respectively. The average fat volume slightly increased between 6 and 12 months, whereas compared with the fat volume, the average muscle volume significantly decreased ($p < 0.001$).
Conclusions: The final overall flap volume in all patients decreased to approximately 25% of the original volume after surgery, which primarily resulted from muscle atrophy. Therefore fat-rich flaps may maintain flap volumes after surgery. MRI is a useful method to evaluate the size and shape of flaps of the head and neck.

Key words: free flap, volume change, chronological change, volumetry, MRI

INTRODUCTION

Oral cancer is the sixth most common cancer worldwide, accounting for approximately 350,000 deaths and 650,000 new diagnoses annually [1]. In addition, oral cancer accounts for approximately 40%–50% of malignancies in South and South-East Asian countries, and its diagnostic rate has continued to steadily increase, even in developed countries [1].

According to established guidelines, surgical resection is the standard therapy for patients with operable oral cancer [2]. However, additional radiation therapy or chemotherapy may be necessary when surgical margins are positive, extracapsular lymph node (LN) spread is identified, or when two or more LNs are positive for metastasis. With regard to surgery, simple tumor resection is recommended if the tumor volume is small, whereas flap reconstruction should be considered if the tumor volume is large, to avoid compromise of postoperative function and/or esthetic appreciation. Approximately 75% of cases require reconstructive surgery to correct defects of the oral cavity [3]. Surgical flap is classified into two categories: pedicle and free flap [4]. The former, with associated vascular anastomosis, is advantageous with regard to flap survival, whereas the free-flap method may cause thrombosis in the feeder artery, thereby resulting in flap necrosis. Furthermore, the free-flap method cannot be applied when a large flap is required. However, this limitation has been resolved by the introduction of a novel free-flap reconstruction technique that facilitates reconstruction of the lesion as well as adjacent tissues.

It is well recognized that the flap volume must be larger than the defect because several factors, such as muscle atrophy, radiation effects, and loss in body weight, may affect the flap volume in the long term [5–8]. Following irradiation, the flap volume decreases in both muscle and fat tissues [5]. Therefore, the flap volume must be experientially determined. In fact, a few authors have measured changes in the overall flap volume for treatment of head and neck cancers [5, 9]. Magnetic resonance imaging (MRI) is a useful method to evaluate flap size and shape, which is clearly visualized due to the signal intensity, primarily of the fat tissue [10, 11]. The aim of the present study was to evaluate the flap volume changes in head and neck by MRI assessment of fat and muscle volume. To our knowledge, this is the first study of flap volumetry of the head and neck using MRI.

PATIENTS AND METHODS

Patients

The study protocol conformed to the principles outlined in the Declaration of Helsinki and was approved by the institutional review board of our institu-

Yuki SAKAMOTO, Department of Oral and Maxillofacial Surgery, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
Tel: +81-463-93-1121 Fax: +81-463-91-5902 E-mail: yukiyama20@hotmail.com

tion. Further, written informed consent was obtained from all patients. Between April 2011 and July 2012, a total of 37 patients underwent reconstructive free-flap intervention for various types of defects of the head and neck at the Department of Oral Surgery, Tokai University School of Medicine (Tokyo, Japan). Of these, 21 (13 males and 8 females; mean age, 67 years; age range, 47–78 years) met the following inclusion criteria: (1) use of reconstructive rectus abdominis myocutaneous free flap (RAMF); (2) no issues regarding flap necrosis or thrombosis; and (3) evaluation of free flap by MRI. However, we excluded 16 patients because of repeated or poor imaging due to artefacts. Accordingly, the study population comprised 21 patients. Tumors originated from the tongue, upper gingiva, lower gingiva, and buccal mucosa in 8, 7, 4, and 2 patients, respectively (Table). Postoperative radiation therapy was administered to 10 patients, directed at the cervical level or the primary lesion in all cases, and the position of the patient's head was set according to Camper's plane and parallel to the floor. Radiation was administered at 6 MeV using an X-ray 3-portal system (50–66 Gy/25–33 fractions daily between Monday and Friday for 6–7 weeks). All flaps were included within the radiation field. MRI and simulation computed tomography (CT) were combined, and the irradiation dose administered to the flap was measured. Patients received irradiation within the initial 6 postoperative weeks, which was continued for 6–8 weeks thereafter. All reconstructions were performed by the same plastic surgeon. Criteria for enrolment were follow-up by MRI at 1 ± 1, 3 ± 1, 6 ± 2, and 12 ± 2 months after surgery.

MR image acquisition, Imaging, and Statistical Analysis

Imaging was performed using a 1.5 T MR scanner (Philips Achieva). Fast spin-echo sequencing was used to obtain T2-weighted images (T2WI) in the axial plane at slice thickness, <5.0 mm; TR/TE, 3800/90; TFE, factor 17; flip angle, 90° ; FOV, 240; matrix, 256 × 256; slices, 20; and slice, BW 180.

In this study, axial T2WIs were used for overall, muscle, and fat volume measurements at each timepoint. Fat and muscle tissues were semiautomatically selected using a computer-operated region of interest (ROI) system on the basis of suitable contrast between the free flap and normal structures (Fig. 1). The thing of the same signal as what was specified by ROI is extracted. Fat and muscle tissues were specified using ROI for every slice, the area was extracted, and the volumes were calculated. Some cases needed correction with a manual. (Fat: 9 cases, Muscle: all cases among 21 cases.) The overall flap, muscle, and fat volumes were measured at 1, 3, 6, and 12 months after surgery, and the average of values recorded by two radiologists were used for analysis. Mann-whitney U test was used to compare to demographic data. Changes in flap content with or without irradiation were also assessed using a mixed-effect regression model. Correlations between body mass index (BMI), serum albumin levels, and changes in flap content were investigated. Correlations of volume change between fat and muscle was also investigated. The Pearson's product-moment correlation coefficient was used to identify significant associations between categorical values. All statistical analyses were performed using SPSS statistical software. Statistical significance was acknowledged for p values of < 0.05.

RESULTS

Surgeries for all 21 patients were performed without complications, and all outcomes were satisfactory. The total flap volume ranged from 26,000 to 152,000 mm3 one month after surgery, and a variation in flap volume with or without irradiation was identified. The average overall flap volume stabilized by 12 months at 76.9% ± 5.2% (Fig. 2). Moreover, the overall muscle volume decreased (final average, 37.1 ± 3.7%). The final average volume of fat stabilized by 12 months at 85.5 ± 5.7%, although the average fat volume slightly increased from 6 to 12 months. Fat-to-muscle ratios varied in all flaps at 1 month (muscle/fat ratio, 0.04–0.96). Muscle/fat ration of all flaps at 1–2 months varied (muscle/fat ratio, 0.02–0.49) (Fig. 3). Muscle volumes significantly decreased compared with fat volumes, despite the varied fat-to-muscle ratios of the flaps ($p < 0.001$). Muscle/fat ratios significantly decreased from 1 to 12 months ($p = 0.012$) (Fig. 3).

There were no significant differences in demographic data among patients with or without a history of irradiation therapy (age, $p = 0.56$; gender, $p = 0.61$; BMI, $p = 0.15$; albumin, $p = 0.31$). The average radiation doses to fat and muscle tissues were 61.1 ± 2.1 and 59.56 ± 1.8 Gy, respectively. The 12-month average volumes of overall flap, muscle, and fat were significantly decreased in irradiated flaps compared with that in nonirradiated flaps ($p < 0.001$) (Fig. 4). No correlation was found between BMI, albumin, and changes in the total flap volume at any timepoint (BMI: 3 months, $p = 0.079$; 6 months, $p = 0.846$; and 12 months, $p = 0.438$; albumin: 3 months, $p = 0.222$; 6 months, $p = 0.287$; and 12 months, $p = 0.265$). No correlation was found between fat volume increase and muscle volume decrease ($p = 0.638$).

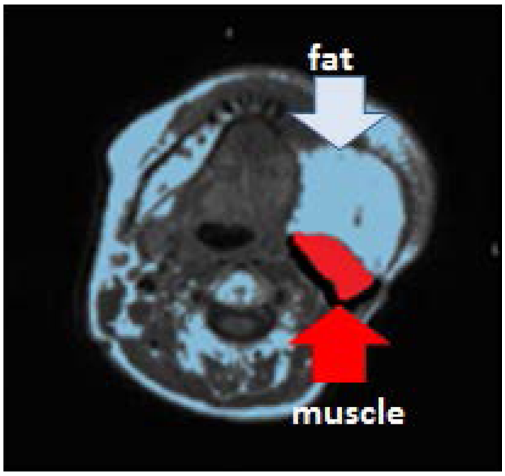
DISCUSSION

Free-flap reconstruction surgery of the head and neck is performed as a standard procedure to maintain residual function and to prevent postoperative complications. Such reconstruction is necessary in oral cancers classified as stages T2, T3, and T4 [12]. Free flaps provide not only safe coverage of large tissue defects but also a cosmetically acceptable appearance [5]. The radial forearm free flap (RFFF), anterolateral thigh flap (ALTF), and RAMF are commonly used in oral cancer surgeries [13]. Traditionally, head and neck defects that require a large amount of soft tissue bulk have been reconstructed with the free myocutaneous rectus abdominis muscle flap [14, 15]. The free muscle-sparing transverse rectus abdominis myocutaneous (MS-TRAM) and deep inferior epigastric perforator (DIEP) flaps involve transferring skin and subcutaneous tissue from the lower abdominal area [16]. To reduce risk of abdominal bulging and hernia, it is important to reserve abdominis muscle. Based on the amount of rectus abdominis muscle spared, Nahabedian *et al.* [17] proposed a classification system

Table Patient and tumor characteristics

Sex	Age, y	Primary tumor site	Postoperative RT	T status	Body Weight (kg)	BMI	albumin (g/dl)
Male	68	upper gingiva	+	T4	53	20.7	4
Male	56	upper gingiva	+	T4	80	24.9	4.1
Male	70	upper gingiva	+	T4	55	20.4	3.7
Male	77	lower gingiva	+	T4	55	20.2	3.7
Male	63	tongue	+	T2	71.5	26.5	4
Male	70	tongue	+	T2	64.5	25.8	3.3
Female	78	buccal	+	T4	42.5	18.8	3.6
Female	70	lower gingiva	+	T4	52	23.7	4.5
Female	47	upper gingiva	+	T4	54	21	4.3
Female	72	upper gingiva	+	T4	55	22	4.4
Male	65	tongue	−	T4	56	20.8	3.3
Male	72	upper gingiva	−	T2	56.3	19.4	3.8
Male	60	upper gingiva	−	T2	61.5	21.2	4
Male	62	tongue	−	T2	63	21.5	4.1
Male	67	upper gingiva	−	T4	53	21.7	4.2
Male	72	tongue	−	T2	67.9	23.8	4.3
Male	76	tongue	−	T4	59	19.9	4
Female	56	lower gingiva	−	T4	58	22.6	4.3
Female	60	tongue	−	T4	54.8	22.5	4.5
Female	63	lower gingiva	−	T4	43.4	18.1	4.3
Female	73	buccal	−	T2	34	16.2	4.7

(+), irradiation; (-), nonirradiation



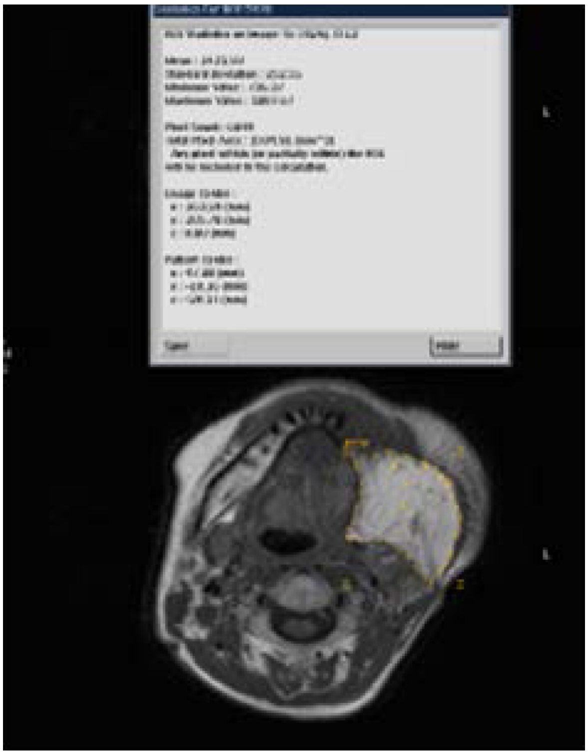


Fig. 1 Fat and muscle imaging. Imaging was performed using a 1.5-T MR scanner (Philips Achieva), with axial T2WI used to measure flap volume. Blue and red zones denote fat and muscle tissues, respectively. After semiautomatic selection by the computer's ROI system, it calculated the ROI range.

of the free TRAM into four types: MS0, in which the full width (partial length) of the rectus abdominis muscle is sacrificed, and MS-1, 2, and 3, in which the lateral segment, the lateral and medial segments, or the entire muscle, respectively, is preserved. Abdominal complications are significantly reduced with this technique compared with those in the pedicled TRAM flap because both lateral innervated muscle and rectus sheath are preserved [18]. In this study, our plastic surgeon used MS-TRAM (MS-0,1,2) flaps. The ratios of muscle and fat displayed individual differences. For example, we constructed MS-0 flaps for women, to compensate for the overall muscle content in females compared with that in males. When a defective space

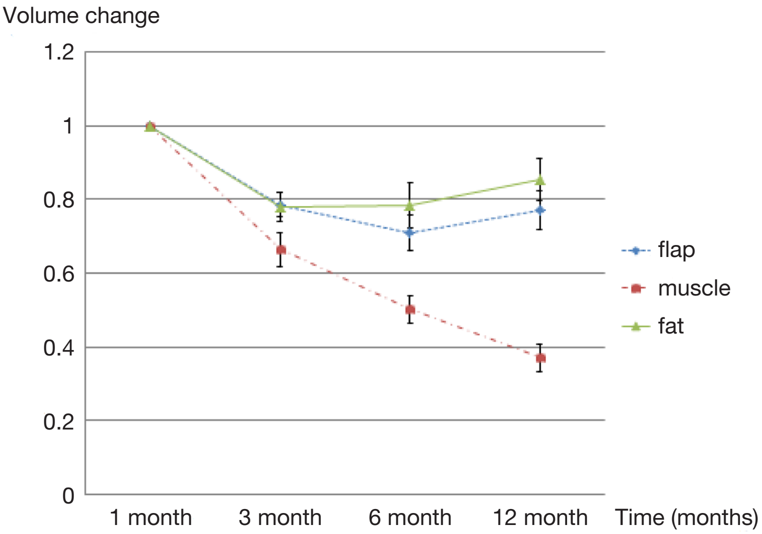


Fig. 2 Average percentages of flap volume for all patients.

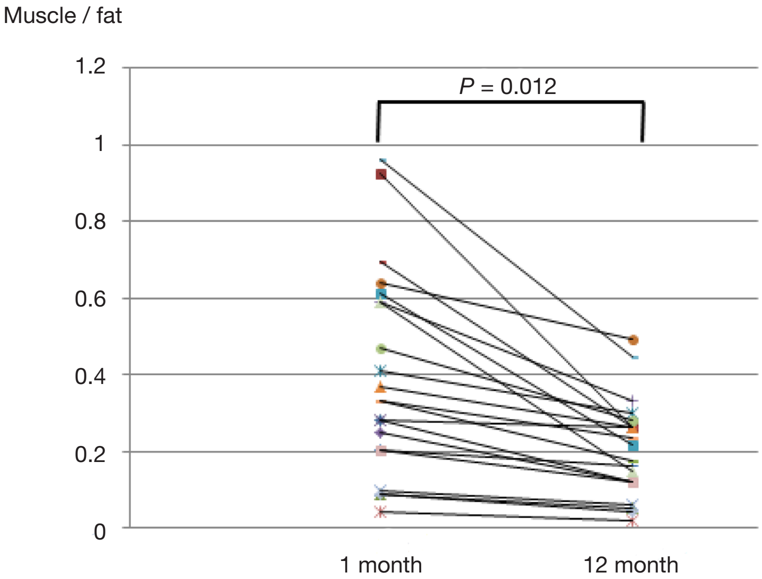


Fig. 3 Fat-to-muscle ratios of all flaps at 1 and 12 months after surgery

was small, or when many muscles were involved, we selected MS-1 or -2 flaps. The MS-TRAM flap remains a widely used procedure because it is technically easier, can be performed earlier than a DIEP flap [15], and fat necrosis occurs less frequently in TRAM flaps [16]. In head and neck reconstruction, the submandibular space must be filled, and muscle tissue presents a useful filler, although it is difficult to separate blood vessels wrapped within muscle fibers to ensure the efficacy and safety of the flap. Therefore, the TRAM flap may still prove to be a more reliable technique despite the development of newer procedures.

Nonetheless, all flaps usually undergo long-term reductions in muscle and fat volume, primarily because of muscle atrophy. Therefore, maintenance of the adequate flap volume is important with regard to swallowing, speech, and esthetic outcomes [19–21]. Empirically, flap size is typically increased by 20%–40% over the actual defect in primary surgery, after considering the reduction in volume caused by muscle atrophy and suturing regardless of wound tension [8, 22, 23].

MRI is an effective method to evaluate postoperative changes and detect new lesions after flap reconstruction [10, 11]. In fact, MRI can help to confirm postoperative changes in hematomas, fluid collection, fat necrosis, and autogenous fat implantation [10]. The contrast zone between flap and residual soft tissue is clearly visualized as low signal intensity line on T1- or T2WIs. The muscle content in a flap is visualized as a heterogenously high signal of fat on T2WIs. Here, we used T2WIs for flap evaluation because of the improved clarity over T1WIs. MRI demonstrated a normal postoperative appearance of benign abnormalities such as skin thickening and fibrosis [11]. Post-radiation therapy fibrosis often displays low signal intensity on T2WIs [11]. Flap volumes could not be accurately measured by CT because of the presence of metal artefacts (Fig. 5); therefore, we used MRI, which offered the advantage of no radiation. Furthermore MRI volumetry is a validated and reliable technique [24].

Yamaguchi *et al.* [9] reported an average final total flap volume of 82.2% using CT volumetry (median follow-up, 28.9 months), which is comparable to the value of 76.5% in our study. Reduction in the flap volume primarily results from muscle atrophy caused by muscle denervation [5, 6], and Yamaguchi *et al.* also reported that the average final muscle volume was

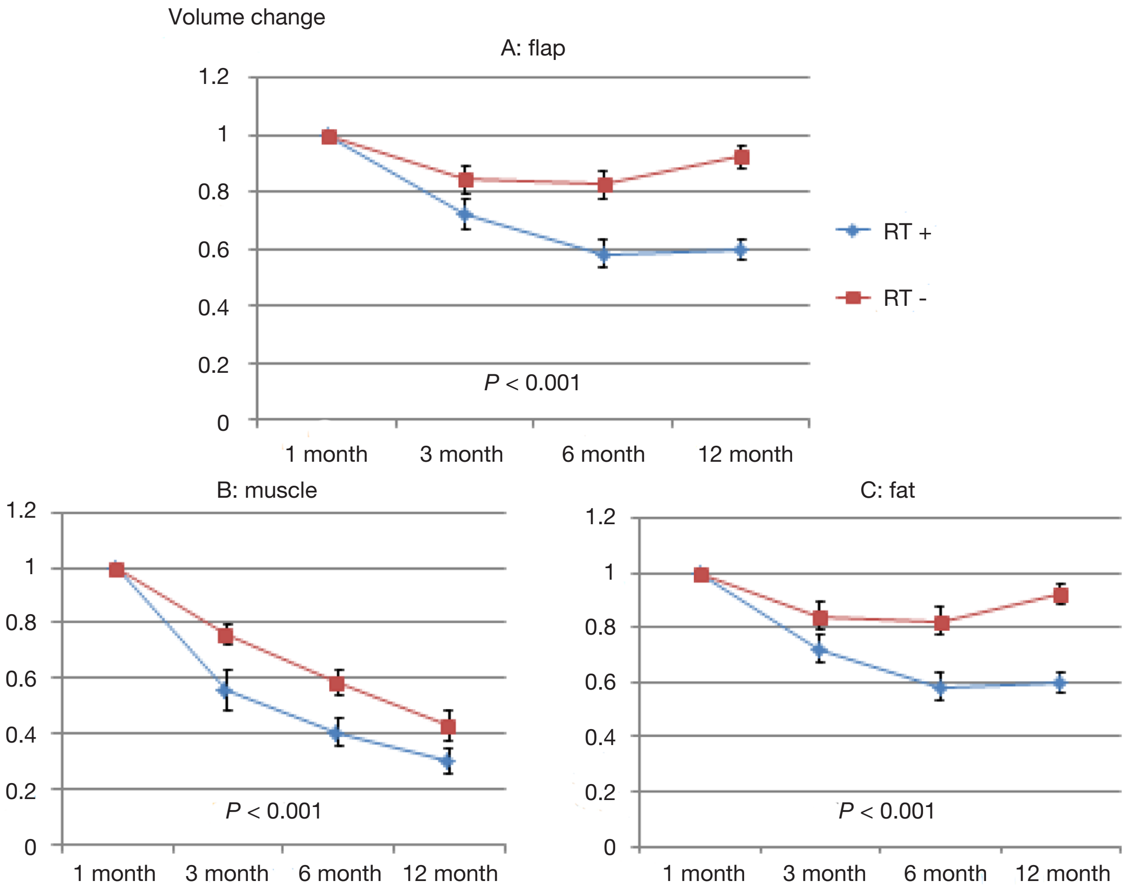
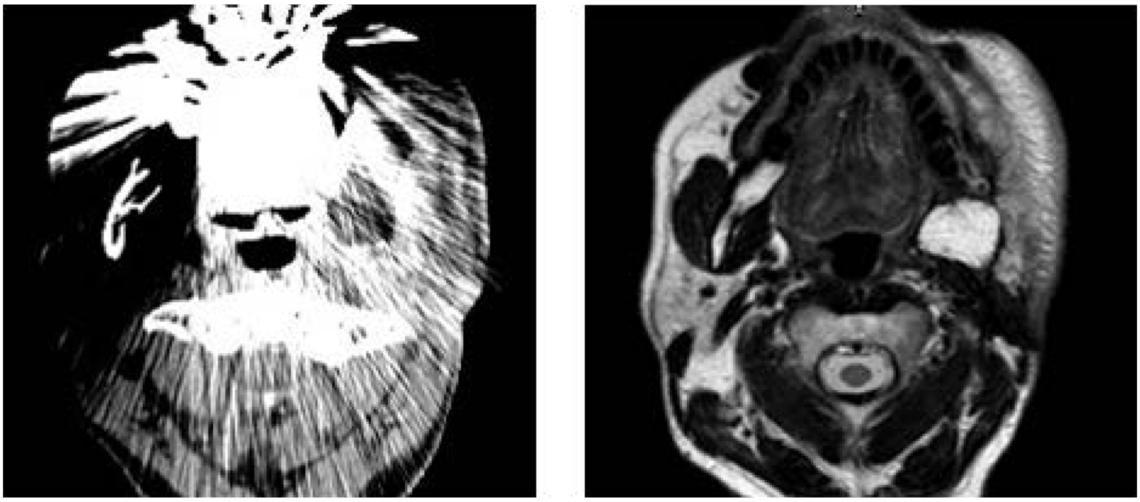


Fig. 4 Volume changes in patients with or without irradiation.
A, flap volume; B, muscle volume; C, fat volume

50% at 12 months after surgery; this having declined in a linear manner and over several years, it eventually retracted to approximately 30% of the original volume [9]. In our study, the average final muscle volume was 37%, which was lower than that reported by Yamaguchi *et al.* Therefore, we speculate that this difference may be attributed to different measurement methods: for volumetry, we used MRI, whereas Yamaguchi *et al.* used CT. However, the use of volumetry by MRI without irradiation is reportedly preferable over volumetry by CT. [24] Another reason could be that the proportion of muscle tissue in all flaps varied between both studies, and flaps with a muscle-rich component tended to shrink more over time [7]. In our study muscle/fat ratio decreased significantly, as evidenced by the increase in fat content at 12 months after surgery. The large increase in the ratio of fat became clear, irrespective of the muscles/fat ratio at 1 month after surgery (Fig. 6).

Although reports of flap fat atrophy are rare [5, 6, 9, 25], Yamaguchi *et al.* [9] reported that the average final fat volume of the flap remained unchanged, whereas Fujioka *et al.* [5] reported an average postoperative fat thickness of 80.1% (range, 60.6%–99.7%) at more than 6 months after surgery. In our study, the average final fat volume was 85.9% at 12 months after surgery, indicating a less marked reduction. The reason for these differences may be related to different measurement techniques to evaluate the flap volume, although volumetry (the method adopted by us) may be more precise compared to 2D measurements. Fat tissue in a free flap barely undergoes atrophy, thereby facilitating long-term stability [26, 27]. We determined that fat tissue in the flap may reveal atrophic changes, according to our results as well as those reported by Fujioka *et al.* Because RAMF contains a considerable amount of muscle and fat tissue, this technique is sufficient to repair larger defects [28]; however, no significant difference was identified with regard to fat volume between RAMF and ALTF in the Yamaguchi study [9]. In our study, different reduction ratios were identified between muscle and fat tissues; therefore, the ratio of fat to muscle should be considered to determine the optimal flap volume.

The flap volume reduction primarily results from muscle atrophy, and fat tissue also shrinks over time. Thus, an optimal flap should be large and rich in fat to maintain its volume. In contrast, relative fat volume tends to increase over time under certain conditions. In our study, the average fat volume slightly increased by 6–12 months (Fig. 4), and in a long-term study by Yamguchi *et al.*, this parameter increased at various timepoints [9]. In general, BMI directly influences fat volume, as pathologically evidenced following weight loss because of symptoms such as anorexia and cachexia [29, 30]. Therefore, we used serum albumin to assess nutritional status. However, although we measured BMI values and serum albumin levels at each timepoint, we could not identify a correlation between either variable and the flap volume. Fat spread to the space from which muscles shrank and it was thought that the volume of fat increased, cor-



A: CT　　　B: MRI T2WI

Fig. 5 Metal archfact in CT.

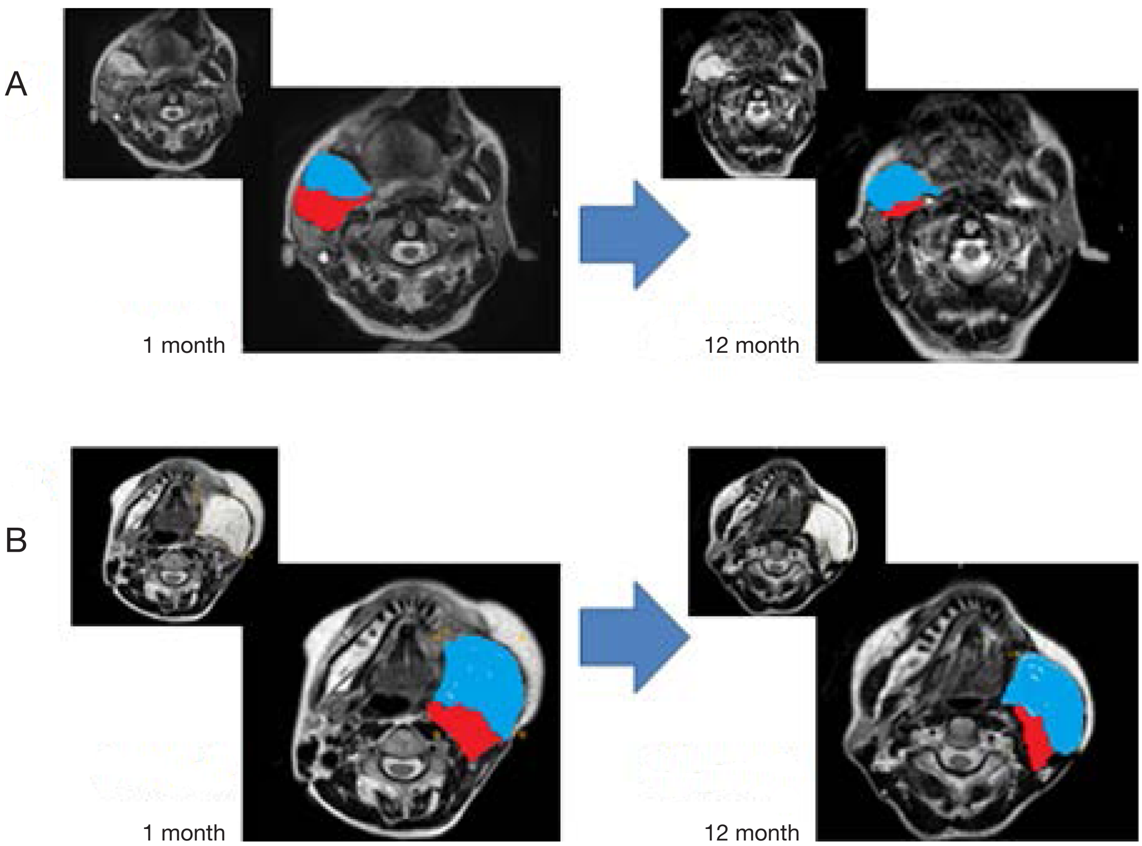


Fig. 6 Changes in flap volume: comparisons for 1 and 12 months after surgery.
A, muscle rich flap; B, fat rich flap.
Blue zone, fat tissue; Red zone, muscle tissue

relation was not observed in the change in fat and muscles. Furthermore, it remains debatable whether postoperative adjuvant irradiation affects the flap volume [5, 9, 23]. Young-Hoon Joo [23] reported a significant correlation between postoperative irradiation and changes in RFFF volume between 3 months and 5 years after surgery. Furthermore, Chatterjee *et al.* [31] reported that postoperative irradiation (45 Gy in 20 fractions) demonstrated no significant effects on breast volume following deep inferior epigastric perforator flap reconstruction. However, in our study, significant differences were observed in the average overall volume of the flap as well as the muscle and fat tissues (lower irradiation flaps). In particular, muscle volume reduction in the irradiated flaps was markedly increased compared with that in the nonirradiated flaps. Although the compared groups were too small for statistical analysis, our findings suggest that irradiation is a significant factor affecting changes in the flap volume.

We acknowledge that this study had certain limitations that must be addressed. First, the patient cohort was small. Second, the 1–2-month follow-up period was short. Last, we analyzed only T stage because we could not measure the actual flap volume. Therefore, we propose that the flap volume should be measured at the point of surgery because the difference in primary sites may affect the flap volume and shape. Hence we plan to consider the unification of primary sites in our next study.

CONCLUSIONS

MRI is a useful method to evaluate the size and shape of flaps of the head and neck. The final flap volumes after surgery decreased overall in all patients to approximately 25% of the original volume, which likely resulted from muscle atrophy.

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