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JCR Year 2024

Plastic Surgery

View title change

ISSN

2292-5503

EISSN

2292-5511

JCR ABBREVIATION

PLAST SURG-CHIR PLAS

ISO ABBREVIATION

Plast. Surg.

Journal information

EDITION

Science Citation Index Expanded (SCIE)

CATEGORY

SURGERY

LANGUAGES	REGION	1ST ELECTRONIC JCR YEAR
Multi-Language	CANADA	2014

Publisher information

PUBLISHER	ADDRESS	PUBLICATION FREQUENCY
SAGE PUBLICATIONS INC	2455 TELLER RD, THOUSAND OAKS, CA 91320	4 issues/year

Journal's performance

Journal Impact Factor

The Journal Impact Factor (JIF) is a journal-level metric calculated from data indexed in the Web of Science Core Collection. It should be used with careful attention to the many factors that influence citation rates, such as the volume of publication and citations characteristics of the subject area and type of journal. The Journal Impact Factor can complement expert opinion and informed peer review. In the case of academic evaluation for tenure, it is inappropriate to use a journal-level metric as a proxy measure for individual researchers, institutions, or articles. Learn more

2024 JOURNAL IMPACT FACTOR	JOURNAL IMPACT FACTOR WITHOUT SELF CITATIONS
0.6	0.4
View calculation	View calculation

Journal Impact Factor Trend 2024

Export

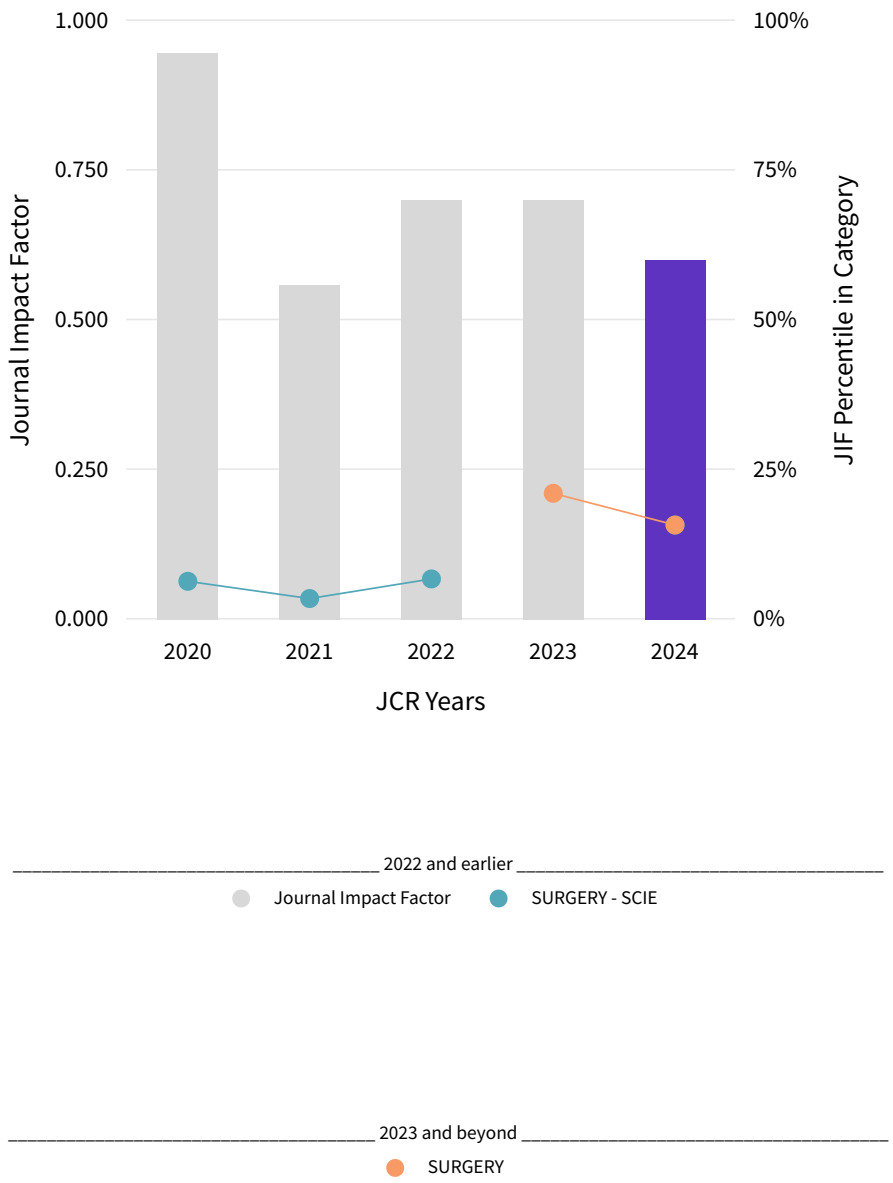
Journal Impact Factor contributing items

Export

Citable items (123) Citing Sources (41)

TITLE	CITATION COUNT
Iliac Crest Bone Graft Harvest for Alveolar Cleft Repair: A Systematic Review…	4
Conversion from Alloplastic to Autologous Breast Reconstruction: Wha…	3

Yardım



Experiences of LGBTQ plus Plastic Surgeons in the US and Canada	3
Prospective Validation of the *Calgary Kids' Hand Rule*: A Clinical Prediction Ru…	3
Readability, Understandability, Usability, and Cultural Sensitivity of Online Patien…	3
What Does Cleft Lip and Palate Care Cost? The Time and Economic-Associated…	3
Closed Incision Negative Pressure Therapy Versus Traditional Dressings fo…	2
Decrease Venous Thromboembolism Without Anticoagulation in Plastic…	2
Main Operating Room Versus Field Sterility in Hand Surgery: A Review of th…	2
Minimal Pain Tumescent Local Anesthesia Injection for Wide Awake Modified Radi…	2

View All in Web of Science

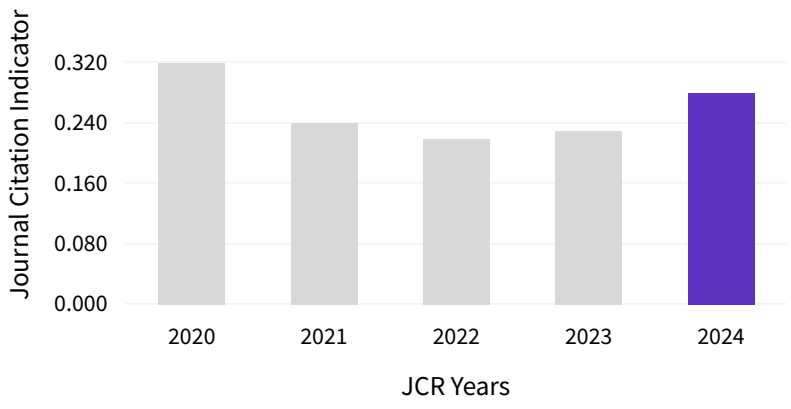
View all years

Journal Citation Indicator (JCI)

Export

0.28

The Journal Citation Indicator (JCI) is the average Category Normalized Citation Impact (CNCI) of citable items (articles & reviews) published by a journal over a recent three year period. The average JCI in a category is 1. Journals with a JCI of 1.5 have 50% more citation impact than the average in that category. It may be used alongside other metrics to help you evaluate journals. Learn more



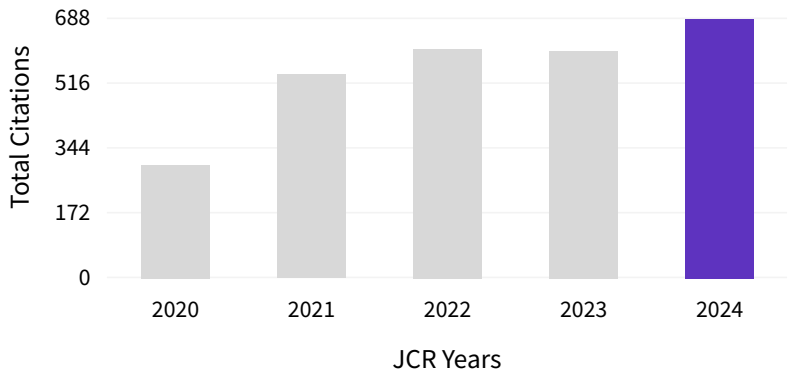
View all years

Total Citations

Export

688

The total number of times that a journal has been cited by all journals included in the database in the JCR year. Citations to journals listed in JCR are compiled annually from the JCR years combined database, regardless of which JCR edition lists the journal.



View all years

Citation distribution

Export

The Citation Distribution shows the frequency with which items published in the year or two years prior were cited in the JCR data year (i.e., the component of the calculation of the JIF). The graph has similar functionality as the JIF Trend graph, including hover-over data descriptions for each data point, and an interactive legend where each data element's legend can be used as a toggle. You can view Articles, Reviews, or Non-Citable (other) items to the JIF numerator. Learn more

ARTICLE CITATION MEDIAN

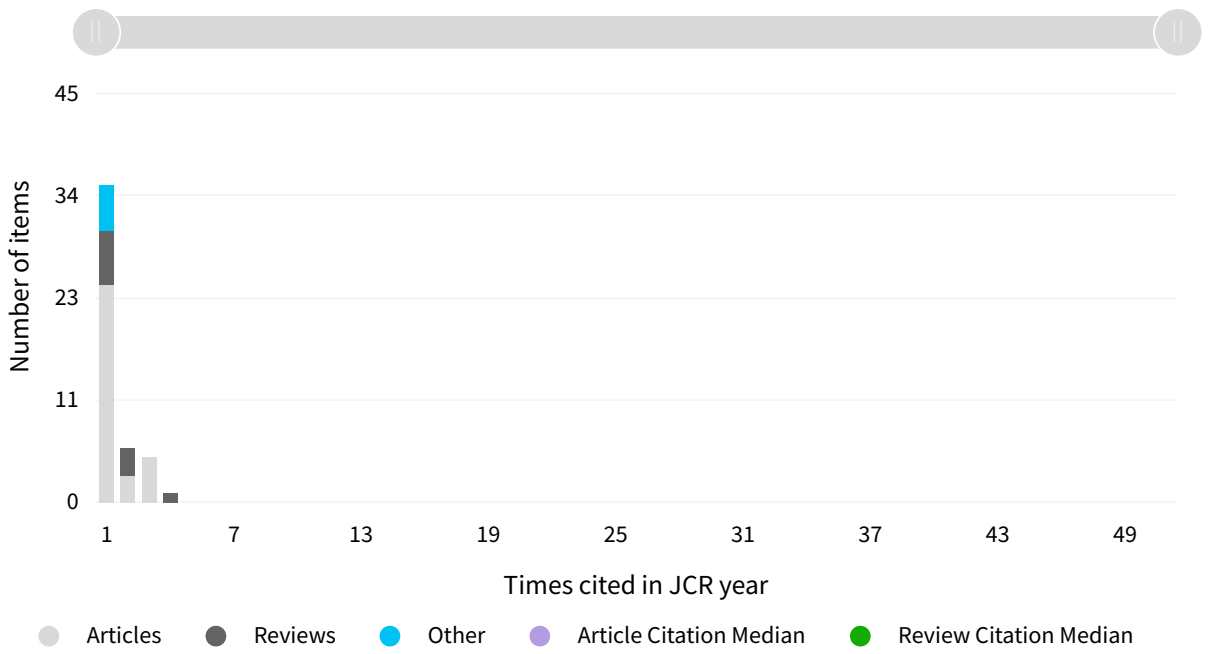
0

REVIEW CITATION MEDIAN

0

UNLINKED CITATIONS

5



TIMES CITED

0

ARTICLES

63

REVIEWS

18

OTHER

41

Open Access (OA)

Export

The data included in this tile summarizes the items published in the journal in the JCR data year and in the previous two years. This three-year set of published items is used to provide descriptive analysis of the content and community of the journal. Learn more

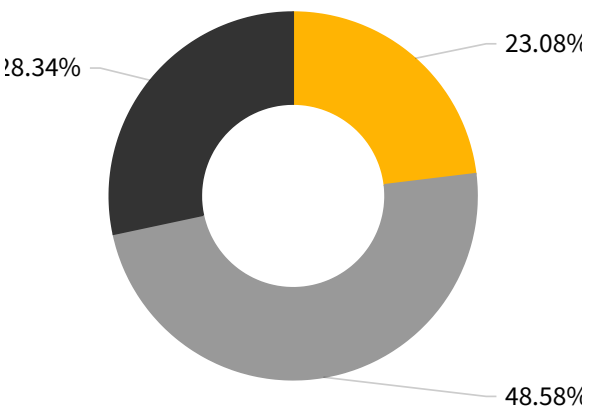
Items

TOTAL CITABLE	% OF CITABLE OA
177	32.20%

CITABLE

GOLD OPEN ACCESS
57 / 23.08%

SUBSCRIPTION AND FREE TO READ
120 / 48.58%



NON-CITABLE

OTHER (NON CITABLE ITEMS)
70 / 28.34%

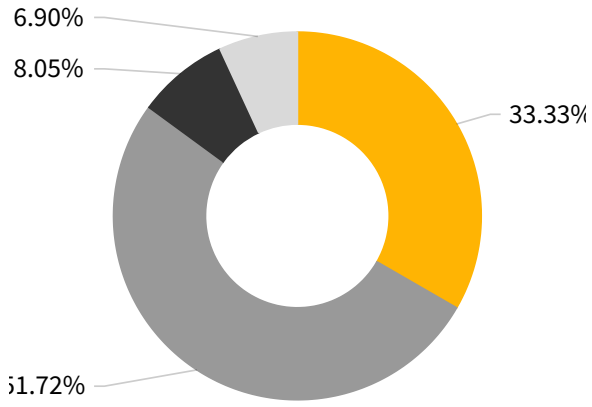
Citations*

TOTAL CITABLE	% OF CITABLE OA
74	39.19%

CITABLE

GOLD OPEN ACCESS
29 / 33.33%

SUBSCRIPTION AND FREE TO READ
45 / 51.72%



NON-CITABLE

OTHER (NON CITABLE ITEMS)
7 / 8.05%

UNLINKED CITATIONS

6 / 6.90%

*Citations in 2024 to items published in [2022 - 2024]

Rank by Journal Impact Factor

Journals within a category are sorted in descending order by Journal Impact Factor (JIF) resulting in the Category Ranking below. A separate rank is shown for each category in which the journal is listed in JCR. Beginning in 2023, ranks are calculated by category.
Learn more

CATEGORY
SURGERY

265/314

JCR YEAR	JIF RANK	JIF QUARTILE	JIF PERCENTILE
2024	265/314	Q4	15.8
2023	231/292	Q4	21.1

Rank by JIF before 2023 for SURGERY

EDITION
Science Citation Index Expanded (SCIE)

JCR YEAR	JIF RANK	JIF QUARTILE	JIF PERCENTILE
2022	199/213	Q4	6.8
2021	206/213	Q4	3.52
2020	198/211	Q4	6.40
2019	193/210	Q4	8.33

Rank by Journal Citation Indicator (JCI)

Journals within a category are sorted in descending order by Journal Citation Indicator (JCI) resulting in the Category Ranking below. A separate rank is shown for each category in which the journal is listed in JCR. Data for the most recent year is presented at the top of the list, with other years shown in reverse chronological order. Learn more

CATEGORY

SURGERY

248/314

JCR YEAR	JCI RANK	JCI QUARTILE	JCI PERCENTILE
2024	248/314	Q4	21.18
2023	253/292	Q4	13.53
2022	240/286	Q4	16.26
2021	233/282	Q4	17.55
2020	213/271	Q4	21.59
2019	211/270	Q4	22.04
2018	212/267	Q4	20.79

Citation network

Cited Half-life

5.6 years

The Cited Half-Life is the median age of the items in this journal that were cited in the JCR year. Half of a journal's cited items were published more recently than the cited half-life.

TOTAL NUMBER OF CITES

688

NON SELF-CITATIONS

641

SELF-CITATIONS

47

Citing Half-life

7.6 years

The Citing Half-Life is the median age of items in other publications cited by this journal in the JCR year.

TOTAL NUMBER OF CITES

1,598

NON SELF-CITATIONS

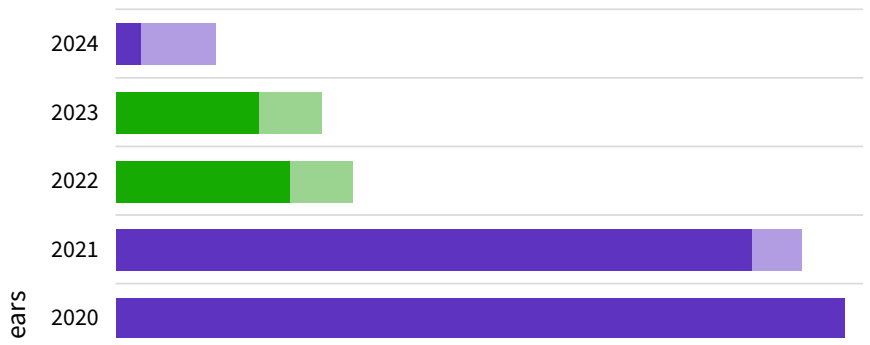
1,551

SELF-CITATIONS

47

Cited Half-life Data | Citing Half-life Data

Export

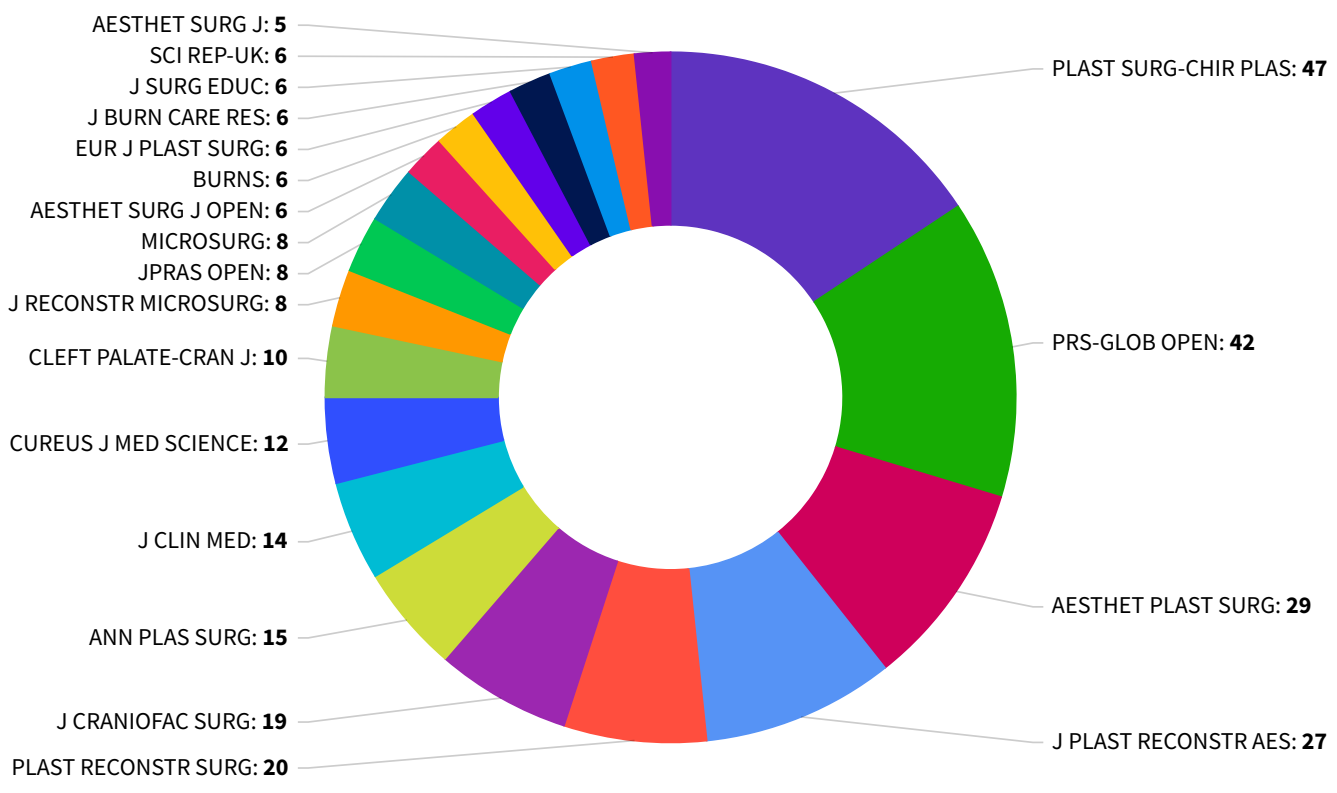


CITED YEAR	# OF CITES FROM 2024	CUMULATIVE %	# OF CITING SOURCES
All years	**688 citations**	**100.00%**	**305 sources**
2024	16 citations	2.33%	5 sources
2023	33 citations	7.12%	23 sources
2022	38 citations	12.65%	24 sources
2021	110 citations	28.63%	70 sources
2020	117 citations	45.64%	81 sources

Journal Citation Relationships

Cited Data Citing Data

Top 20 journals citing PLAST SURG-CHIR PLAS by number of citations



Content metrics

Source data

This tile shows the breakdown of document types published by the journal. Citable Items are Articles and Reviews. For the purposes of calculating JIF, a JCR year considers the publications of that journal in the two prior years. Learn more

54 total citable items

	ARTICLES	REVIEWS	COMBINED(C)	OTHER DOCUMENT TYPES(O)	PERCENTAG
NUMBER IN JCR YEAR 2024 (A)	48	6	54	24	69%
NUMBER OF REFERENCES (B)	1,157	304	1,461	137	91%
RATIO (B/A)	24.1	50.7	27.1	5.7	

Average JIF Percentile

Export

The Average Journal Impact Factor Percentile takes the sum of the JIF Percentile rank for each category under consideration, then calculates the average of those values. Learn more

ALL CATEGORIES AVERAGE
15.8

SURGERY
15.8

Contributions by organizations

Export

Organizations that have contributed the most papers to the journal in the most recent three-year period. Learn more

RANK	ORGANIZATION	COUNT
1	UNIVERSITY OF BRITISH COLUMBIA	40
2	UNIVERSITY OF TORONTO	37
3	MCMASTER UNIVERSITY	31
4	MCGILL UNIVERSITY	27
5	BC CHILDREN'S HOSPITAL	16
6	UNIVERSITY OF CALGARY	15
7	UNIVERSITY OF	14

Contributions by country/region

Export

Countries or Regions that have contributed the most papers to the journal in the most recent three-year period. Learn more

RANK	COUNTRY / REGION	COUNT
1	CANADA	140
2	USA	78
3	ENGLAND	7
-	TURKIYE	7
5	SAUDI ARABIA	4
6	MEXICO	3
-	SOUTH KOREA	3
8	GERMANY (FED REP GER)	2
-	INDIA	2

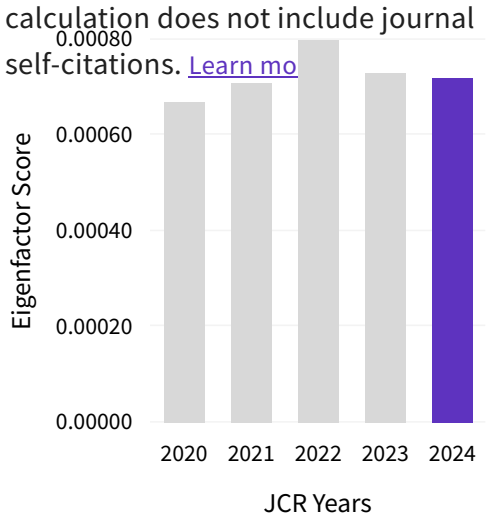
Additional metrics

Eigenfactor Score
0.00072

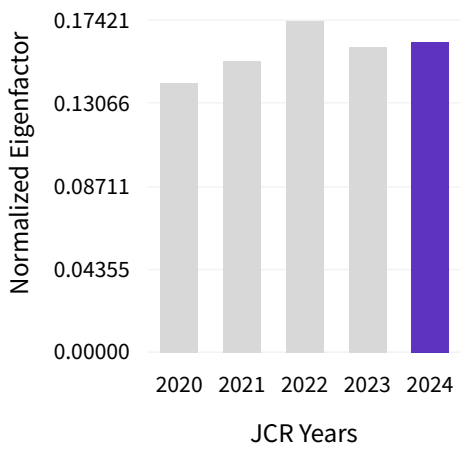
Normalized Eigenfactor
0.16308

Article influence score
0.298

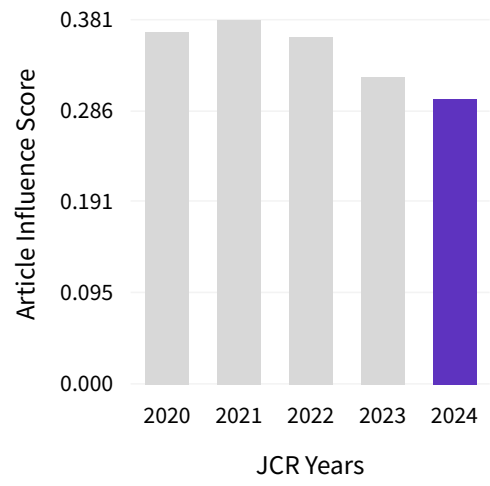
The Eigenfactor Score is a reflection of the density of the network of citations around the journal using 5 years of cited content as cited by the Current Year. It considers both the number of citations and the source of those citations, so that highly cited sources will influence the network more than less cited sources. The Eigenfactor calculation does not include journal self-citations. Learn mo



The Normalized Eigenfactor Score is the Eigenfactor score normalized, by rescaling the total number of journals in the JCR each year, so that the average journal has a score of 1. Journals can then be compared and influence measured by their score relative to 1. Learn more



The Article Influence Score normalizes the Eigenfactor Score according to the cumulative size of the cited journal across the prior five years. The mean Article Influence Score for each article is 1.00. A score greater than 1.00 indicates that each article in the journal has above-average influence. Learn more

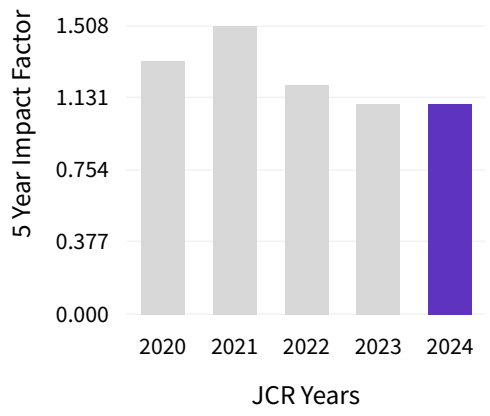


5 Year Impact Factor

1.1

View Calculation

The 5-year Impact Factor is the average number of times articles from the journal published in the past five years have been cited in the JCR year. It is calculated by dividing the number of citations in the JCR year by the total number of articles published in the five previous years. Learn more

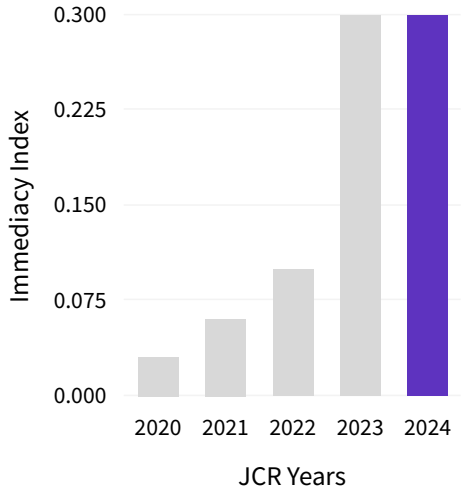


Immediacy Index

0.3

View Calculation

The Immediacy Index is the count of citations in the current year to the journal that reference content in this same year. Journals that have a consistently high Immediacy Index attract citations rapidly. Learn more



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Intended for healthcare professionals

Sage Journals

Plastic Surgery

Impact Factor: **0.6**
5-Year Impact Factor: **1.1**

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Experimental Investigation into the Effect of Variable Inflation Intervals on Capsule Thickness in Tissue Expander

Étude expérimentale de l'effet d'intervalles d'inflation variables sur l'épaisseur de la capsule dans l'expanseur tissulaire

Buket Dursun Coban, MD[1], Can Ilker Demir, MD[2], Emrah Kagan Yaşar, MD[3], Ismail Tekfiliz, MD[3], Murat Sahin Alagoz, PhD, MD[3], and Busra Yaprak Bayrak, MD[4]

Abstract

Introduction: Increasing the thickness of the capsule around the tissue expander, as in breast reconstruction complicates the expansion process and increases the time to achieve the required flap size. The aim of this study was to investigate the effect of changes in inflation intervals and amounts on the capsule thickness around the tissue expander. **Methods:** Fifteen adult rats were divided into 3 groups, and 25 cc elliptical tissue expanders were placed on the back of each, and inflated with 5 cc saline. Expanders were inflated daily in Group 1, every 3 days in Group 2, and every 10 days in Group 3. Inflation was stopped, then expanders were removed and skin flaps were harvested after the results of the expansion were measured. Biopsies containing skin and capsule tissue were evaluated by histomorphometry and immunohistochemistry. **Results:** Skin flaps were measured as 81 cm^2 in Group 1 and 89.3 cm^2 in both Groups 2 and 3. When capsule thickness and number of vessels were examined; the thickest capsule was found in Group 2 while Group 3 had the densest vascularization. On histopathological examination of the biopsies, no significant difference was found between groups, except for the histiocyte density, which was the lowest in Group 1 and the highest in Group 3. **Conclusions:** This experiment showed that inflating tissue expander in small amounts at frequent intervals decreased the thickness of the capsule but it resulted in smaller skin flaps. Thus, it may be beneficial to adopt this protocol in some patients, for example in patients who are predicted to have increased capsule thickness due to the effect of radiotherapy and/or chemotherapy, or who are prone to fibrosis. Additionally, in patients whose flap size is important, it may be reasonable to inflate the tissue expander at less frequent intervals and in relatively large volumes for preventing flap loss and avoiding an increase in capsule thickness.

Résumé

Introduction: L'accroissement de l'épaisseur de la capsule entourant l'expanseur tissulaire utilisé pour la reconstruction mammaire complique le processus d'expansion et rallonge la période nécessaire pour obtenir un lambeau de la dimension voulue. La présente étude visait à examiner l'effet des changements aux intervalles d'inflation et à l'épaisseur de la capsule autour de l'expanseur tissulaire. **Méthodologie:** Quinze rats adultes ont été divisés en trois groupes. Des expanseurs tissulaires elliptiques de 25 cc ont été placés sur le dos de chacun d'eux et gonflés à l'aide de 5 cc de chlorure de sodium. Les expanseurs ont été

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Email: buketdursun@gmail.com

gonflés tous les jours dans le groupe 1, tous les trois jours dans le groupe 2 et tous les dix jours dans le groupe 3. L'inflation a été interrompue, puis les expanseurs ont été retirés, et les lambeaux cutanés ont été prélevés après la mesure de l'expansion. Des biopsies contenant de la peau et des tissus capsulaires ont été évaluées par histomorphométrie et immunohistochimie. **Résultats:** Les lambeaux cutanés mesuraient 81 cm^2 dans le groupe 1 et 89,3 cm^2 dans les groupes 2 et 3. À l'examen de l'épaisseur capsulaire et du nombre de vaisseaux, la capsule la plus épaisse se trouvait dans le groupe 2, tandis que le groupe 3 présentait la vascularisation la plus dense. À l'examen histopathologique des biopsies, les chercheurs n'ont observé aucune différence significative entre les groupes, sauf la densité des histiocytes, qui était plus faible dans le groupe 1 et plus élevée dans le groupe 3. **Conclusion:** Cette expérience a révélé que de petites inflations de l'expanseur tissulaire à de fréquents intervalles réduisaient l'épaisseur de la capsule, mais produisaient de plus petits lambeaux cutanés. Il peut donc être bénéfique d'adopter ce protocole chez certains patients, par exemple lorsqu'on leur prédit une plus grande épaisseur capsulaire en raison de l'effet de la radiothérapie ou de la chimiothérapie ou d'une prédisposition à la fibrose. De plus, chez les patients dont la dimension du lambeau est importante, il peut être raisonnable de gonfler l'expanseur tissulaire à des intervalles moins fréquents et à des volumes relativement importants pour prévenir la perte du lambeau et éviter l'augmentation de l'épaisseur capsulaire.

Keywords
tissue expander, capsular contracture, breast reconstruction, flap

Mots-clés
contracture capsulaire, extenseur tissulaire, lambeau, reconstruction mammaire

Introduction

Tissue expansion has revolutionized reconstructive surgery by enabling the creation of additional tissue through a controlled process of mechanical stretching, thus minimizing donor site morbidity and improving tissue compatibility. This technique leverages the body's natural ability to respond to mechanical stress, offering a unique solution to complex defect repairs.[1]

However, the journey from tissue expansion to successful reconstruction is not without challenges. A critical issue encountered, especially in breast reconstruction, is the formation of a thick fibrous capsule around the expander, leading to complications such as capsular contracture. This phenomenon, with an incidence rate ranging from 13.7% to 45%, can severely impede the aesthetic and functional outcomes of the reconstruction.[2] Capsule thickness not only hampers the tissue expansion process but also limits the size and mobility of the flaps, thus compromising the desired reconstructive results.[3,4]

In response to these challenges, extensive research has explored various pharmacological interventions to mitigate capsule formation, including the use of botulinum toxin, leukotriene antagonists, steroids, and estradiol. Despite these efforts, the optimal approach to minimizing capsule thickness remains elusive.[5–9]

This study was designed to address this gap by investigating a novel aspect of tissue expander use the impact of inflation intervals and volume changes on capsule thickness. We hypothesized that varying the time between inflation sessions and adjusting the inflation volumes would significantly influence capsule formation, thereby providing new insights into optimizing the tissue expansion process. Using an animal model, we aimed to elucidate the effects of these variables on capsule thickness, with the ultimate goal of enhancing reconstructive outcomes.

Methods

This study was conducted following the approval of the Animal Research Ethical Committee of Kocaeli University (Project No: 2021/01). Fifteen young adult Sprague-Dawley rats (mean age: 8 weeks, weight: 250-350 g) were housed individually under controlled conditions: a 12-hour light/dark cycle (lights on at 08:00), temperature maintained at 22 ± 2 °C, and humidity at 60% to 70%.

Experimental Model

The rats were randomly allocated into 3 groups ($n = 5$ per group). The objective was to inflate the tissue expanders with varying volumes of saline over a 30-day period, differing in the frequency and volume of inflation. Group 1 received 1 cc of saline daily, Group 2 received 3 cc of saline every 3 days, and Group 3 received 10 cc of saline every 10 days.

Surgical Procedure and Tissue Expansion Protocols

Anesthesia was administered using an intraperitoneal injection of 50 mg/kg ketamine and 10 mg/kg xylazine HCl. Prophylaxis was provided with a single dose of cefazolin sodium (30 mg/kg). Each rat had a 25 cc (6×4 cm) silicone tissue expander placed subcutaneously on the back. The procedure involved positioning the rats prone, with limbs abducted at 120°, shaving and preparing the surgical area, and marking a 7×7 cm area with the top

point at the interscapular line (Figure 1A). Adaptation sutures were placed at the lateral and superior edges, followed by a 3 cm horizontal incision in the right lumbar region to access the subcutaneous tissue and panniculus carnosus (Figure 1B). Blunt dissection was used to create a pocket under the marked 7 × 7 cm skin island for the tissue expander and its port, which were inserted under sterile conditions (Figure 1C). The incision was closed with 4/0 silk sutures, and the operation was completed with appropriate dressing (Figure 1D). Each expander was initially inflated with 5 cc of saline perioperatively (Figure 2A).

Over the subsequent 30 days, the expanders were periodically inflated according to the group-specific protocols. Inflation was stopped on day 30 in all groups, reaching a final volume of 35 cc (Figure 2B). The area of expansion was calculated using the formula "Area = Width×Length" based on measurements taken from the fixed sutures (Figure 2C). On day 31, tissue expanders were removed, and histopathological and immunohistochemical analyses were performed on the capsule tissues surrounding the expanders.

Histopathological Examination

After achieving the maximum targeted volume of 35 cc, tissue samples were collected on day 31. The rats were re-anesthetized, and the previously marked surface area on the back was remeasured to calculate changes in the area (Figure 2C). The expanded skin was divided into 4 quadrants, and full-thickness biopsies of 4 cm^2 (2 × 2 cm) were taken from the left upper and right lower quadrants (Figure 3A). The saline was drained from the expanders, which were then removed (Figure 3B). Following macroscopic evaluation and photography (Figure 3C), tissues were fixed in 10% formalin for histopathological examination.

Tissue samples were processed in 10% formalin for 24 h, embedded in paraffin, and sectioned into 4 μm slices. Hematoxylin-eosin (H&E) staining was performed. Histopathological evaluation assessed capsule tissue, dense regular connective tissue, loose connective tissue content, granulation tissue, inflammatory cell infiltration (neutrophils and lymphocytes), fibroblast counts, and neovascularization. Each parameter was graded on a scale from 0 to 3 (0 = absent; 1 = mild; 2 = moderate; 3 = severe).[10] Capsule thickness was measured in micrometers at 4 different sites, and the mean thickness was calculated (Figure 4).

Immunohistochemical Analysis

Immunohistochemical staining was conducted on 4 μm thick sections using CD68 (CL1338, monoclonal, and AMAB90873) and smooth muscle actin (SMA; SP171, monoclonal, and SAB5500002) antibodies. Staining was performed using a Ventana automated device (Roche Ventana) with Optiview and Ultraview DAB kits. Tonsil tissue served as a positive external control. The percentage of capsular area and vascular structures stained with SMA, and the percentage of histiocytes stained with CD68, were quantified automatically using an Olympus BX50 microscope.

Statistical Evaluation

Statistical analyses were performed using SPSS, version 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to assess normal distribution. Numerical variables are presented as medians (25th-75th percentile, interquartile range). Group differences were analyzed using Kruskal-Wallis one-way ANOVA and Dunn's multiple comparison test for nonnormally distributed data. A P-value <.05 was considered statistically significant.

Results

Flap Surface Area

The mean resulting skin surface area, as defined by the marking sutures, was 81 cm^2 in Group 1, corresponding to a 65.3% increase in area. In Groups 2 and 3, the mean resulting surface area was identical at 89.3 cm^2, representing an 82.2% increase in both groups (Figure 5). Although Groups 2 and 3 showed a greater percentage increase compared to Group 1, intergroup comparisons revealed no statistically significant differences in the surface area expansion among the 3 groups (P > .05). Detailed results and statistical analyses are presented in Table 1, which illustrates the distribution and variability of surface area changes across the groups.

Histological Examination

The median number of vessels identified per high-power field was 70 in Group 1, 90 in Group 2, and 95 in Group 3, with no statistically significant differences observed among the groups (P = .15) (Figure 6A). The angiogenic response, as measured by vessel density, appeared to be slightly more pronounced in Groups 2 and 3, possibly reflecting the effects of different inflation protocols on vascular proliferation.

The greatest median capsule thickness was observed in Group 2, with a median value of 1000 μm (IQR: 950-1050 μm). Group 1 exhibited a median thickness of 600 μm (IQR: 580-620 μm), while Group 3 had a median thickness of 720 μm (IQR: 700-740 μm) (Figure 6B). Despite the noticeable differences in median values, the statistical comparison did not indicate significant differences in capsule thickness between the groups (P = .09). These findings suggest that the interval and volume of inflation may influence capsule thickness to some extent, although the variability within groups could mask statistical significance.

Histopathological scoring of parameters such as PMNL density, degree of fibrosis (Figure 6C), inflammatory signs, increased fibroblast activity, and lymphocyte density revealed no significant differences between the groups (P > .05 for all comparisons). However, histiocyte density analysis demonstrated a clear and significant increase in Groups 2 and 3

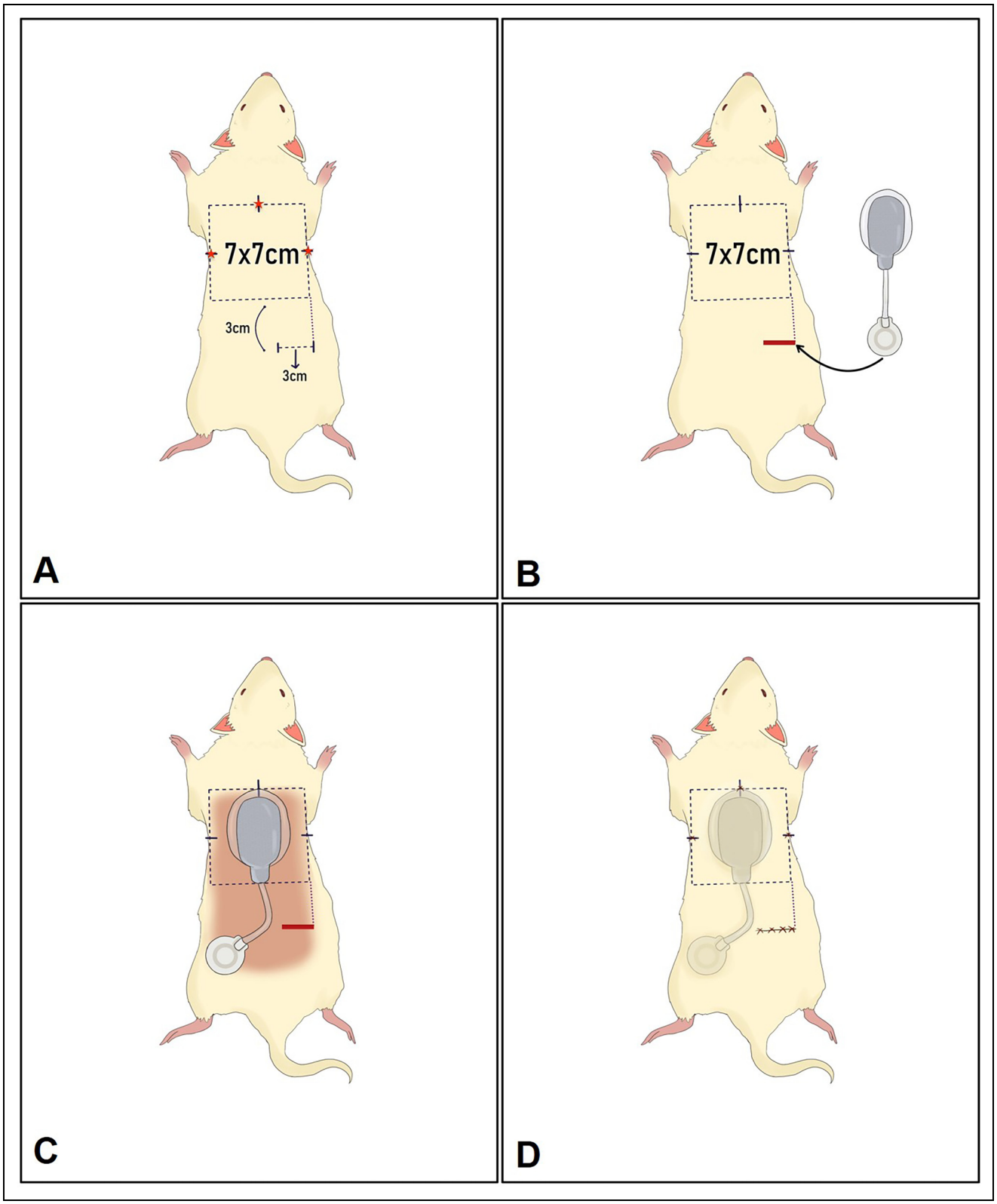


Figure 1. A schematic representation of the operation. (A) A 7 × 7 cm area was marked on the rat's back, with the highest point at the level of the interscapular line and a 3 cm horizontal incision was planned from 3 cm caudal to the inferior border of this area. Adaptation sutures were placed at the midpoint of both the lateral and cranial edges of the marked region (star). (B) A suitable pocket was prepared for the tissue expander and its port by entering through the planned incision. (C) The tissue expander was placed in the prepared pocket. (D) The incision was sutured primarily.

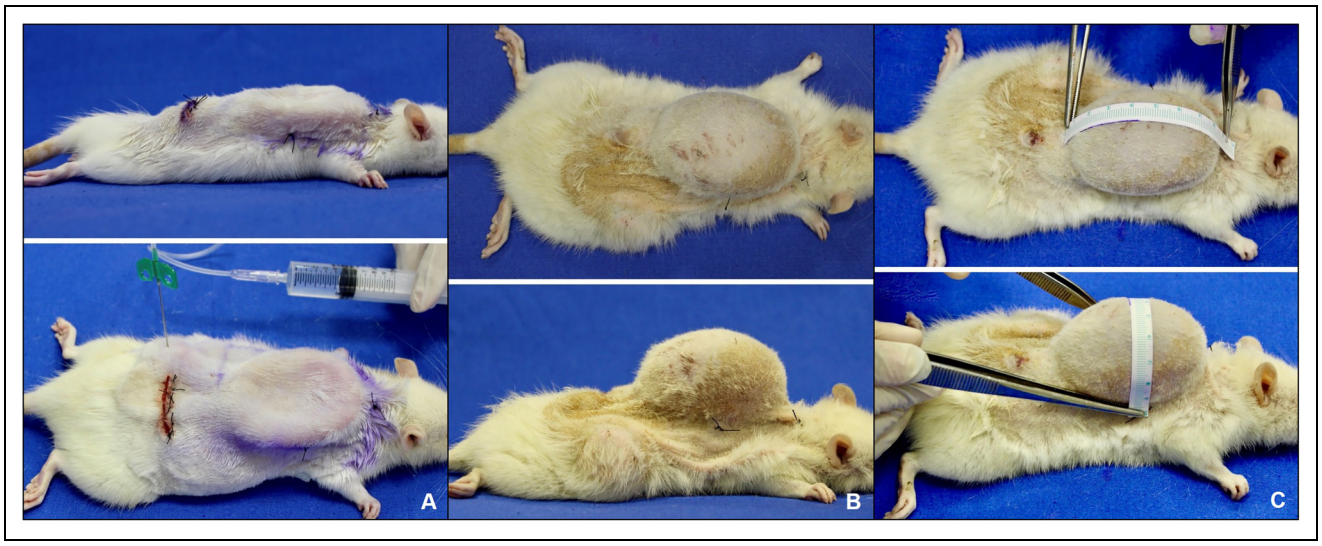


Figure 2. (A) Lateral view of the inserted tissue expander and the tissue expander was inflated peroperatively through its port using a butterfly needle. (B) Image of tissue expander with 35 cc final volume. (C) At the end of the expansion process, the length and width of the expanded tissue were measured.



Figure 3. (A) An area of 4 cm^2 was planned from the left upper and right lower quadrants for capsule and skin biopsy. (B) In order not to damage the tissue expander, the tissue expander was removed before biopsies were taken. (C) Representation of the capsule tissue in the biopsy material.

compared to Group 1 (Figure 7, Table 2). Group 1 had no detectable histiocyte presence (score 0), while Group 2 had a score of 1 (mild presence) and Group 3 had a score of 2 (moderate presence) ($P = .025$). The differential presence of histiocytes may indicate a varying degree of chronic inflammatory response or foreign body reaction related to the inflation protocols used.

Immunohistochemical analysis showed varying expression levels of CD68 and SMA across the groups. While CD68 staining, indicative of macrophage activity, was minimal in Group 1, it was more pronounced in Groups 2 and 3, correlating with the histiocyte density findings (Figure 6D). SMA staining revealed consistent smooth muscle actin presence across all groups, with no significant differences in the percentage of stained capsular area or vascular structures (Figure 8). These findings suggest that while the overall inflammatory and fibrotic responses were similar, the presence of macrophages may be more sensitive to changes in inflation timing and volume.

Discussion

In postmastectomy alloplastic breast reconstruction, one of the major problems seen is contraction of the capsule, reported to affect between 13.7% and 45% of patients.[2] It has been reported that increasing the thickness of the capsule around the tissue expander is one of the most important factors affecting the final success of the tissue expansion process.[3] Increasing the thickness of the capsule not only complicates the tissue expansion process, but also reduces the size and movement of the flaps provided after expansion, making it difficult to achieve the desired reconstructive and aesthetic result.[4] For breast reconstruction surgery, this increase in capsule thickness may

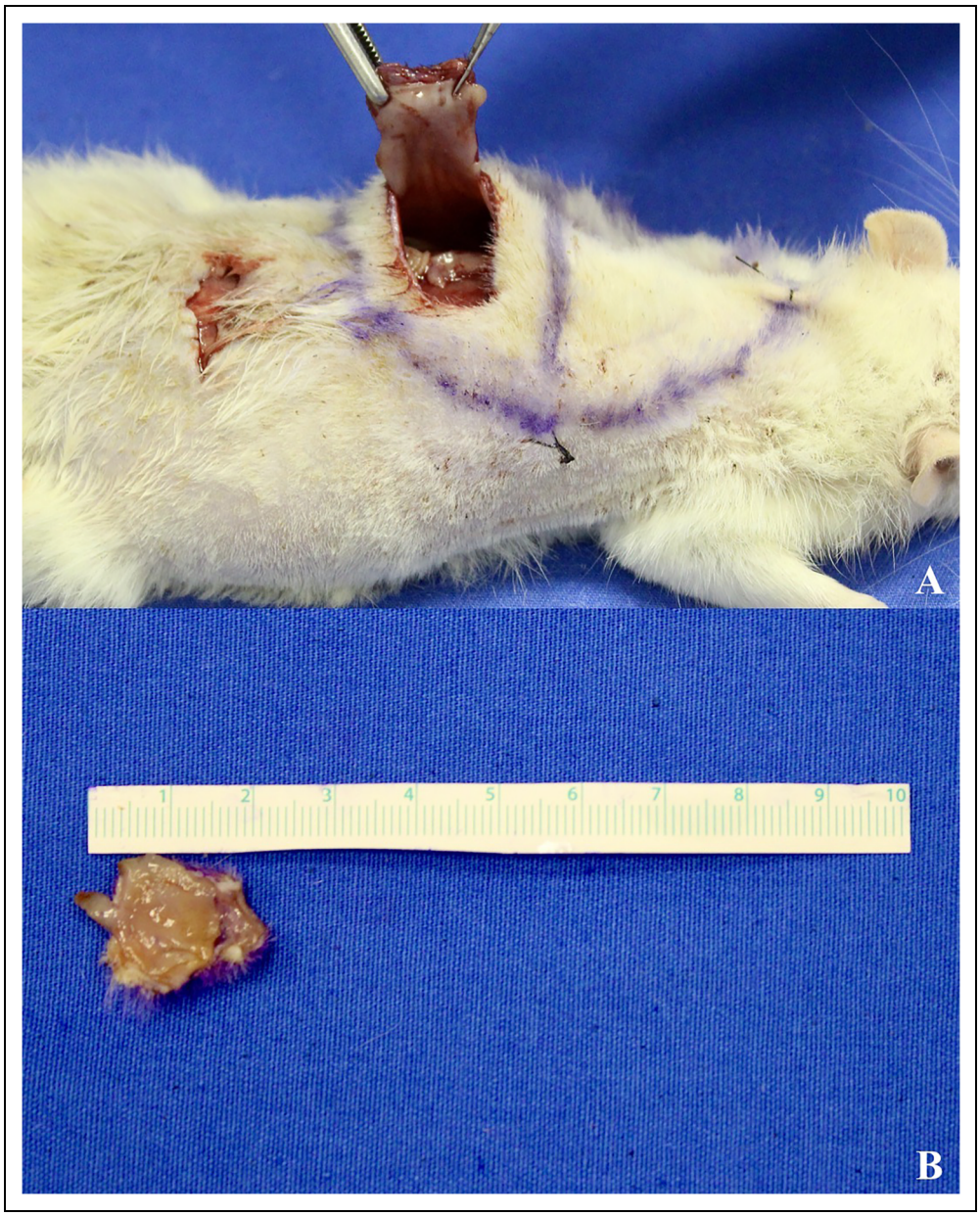


Figure 4. (A) The preparation of skin and capsule tissue biopsies on the back of rats. (B) The capsule biopsies were measured and prepared for microscopy examination.

result in an insufficiently sized pouch for the permanent prosthesis. Then, due to being unable to place the desired prosthesis, the breast projection may be inadequate. In addition, contracture around the implant may occur later and revision surgeries may be required due to this contraction.[3,4]

Capsule formation is a natural reaction of the body to foreign bodies. Capsular contraction may occur as the capsule tissue increases in thickness and becomes fibrotic. Even though the relationship between capsule thickness and capsular contracture has not yet been fully elucidated, several studies have demonstrated that Baker III and IV capsules are thicker than Baker I and II capsules.[11] Many factors have been suggested to cause this contraction but the exact mechanism is, as yet, unknown.[12,13] The implant surface structure has been shown to affect the formation of capsular contracture and textured surface implants are less likely to cause capsular contracture than smooth surface implants.[5,14] However, in recent years, it has been found that the probability of developing implant-associated anaplastic large cell lymphoma (BIA-ALCL) is higher in textured implants than in smooth-surfaced implants.[15] Since textured implants are associated with this higher risk of lymphoma, smooth surface implants have again become more widely used. This has resulted in a renewed interest in understanding and preventing capsule

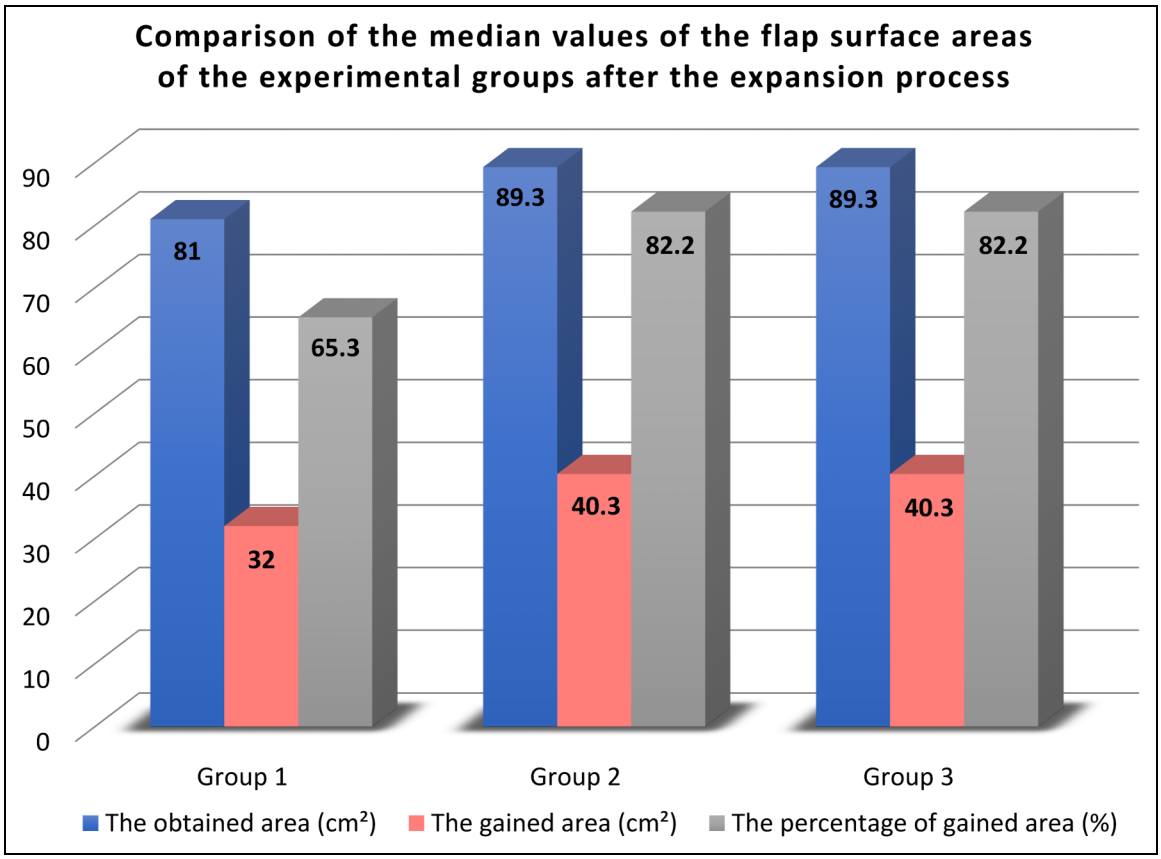


Figure 5. Comparison of the median values of the flap surface areas of the experimental groups after the expansion process.

Table 1. After the Experimental Tissue Expansion Procedure, the Length and Width of the Expanded Skin Flaps Were Measured and the Resulting Area, the Gained Area, and the Percentage Increased Area Were Calculated and Compared.

		Length (cm)	Width (cm)	Resulting area (cm^2)	The gain in area (cm^2)	Percentage gained area (%)
Group 1	Median	9	9	81	32	65.30
	Mean	8.9	9.14	81.6	32.6	66.5
	IQR	8.35-9.40	8.75-9.60	73.10-90.40	24.10-41.40	49.15-84.45
Group 2	Median	9.4	9.5	89.3	40.3	82.2
	Mean	9.32	9.68	90.4480	41.4480	84.54
	IQR	8.85-9.75	9.05-10.40	80.095-101.375	31.095-52.375	63.40-106.85
Group 3	Median	9.5	9.5	89.3	40.3	82.2
	Mean	9.56	9.48	90.73	41.73	85.132
	IQR	9.40-9.75	8.70-10.25	82.175-100.000	33.175-51.000	67.695-104.035
	*P	.191	.440	.331	.331	.331

Abbreviation: IQR, interquartile range.
Groups were statistically compared. A statistically significant difference was not detected (* $P > .05$).

contraction. Many studies have been carried out to try to make the tissue expansion process safer and in a shorter time, and many pharmacological agents have been tried.[6–9,16]

It is thought that myofibroblasts (contractile fibroblasts) are a significant factor in causing capsular contracture.[17,18] Thus there has been much research into the efficacy of anti-contractile drugs on capsule thickness.[18–20] Tang et al[20] investigated the use of topical versus catheter-injected papaverine in a minipig model with tissue expanders placed on the animals' backs. The increase in area was greatest in the animals receiving topical papaverine, and the collagen and fibroblast alignment was more regular in capsule biopsies from this group.

Contractile fibroblasts arise in connective tissue as a response to mechanical stress and tend to resist applied pressure and force. In wound healing pathophysiology, fibroblasts are the dominant cell type from the third day until the second

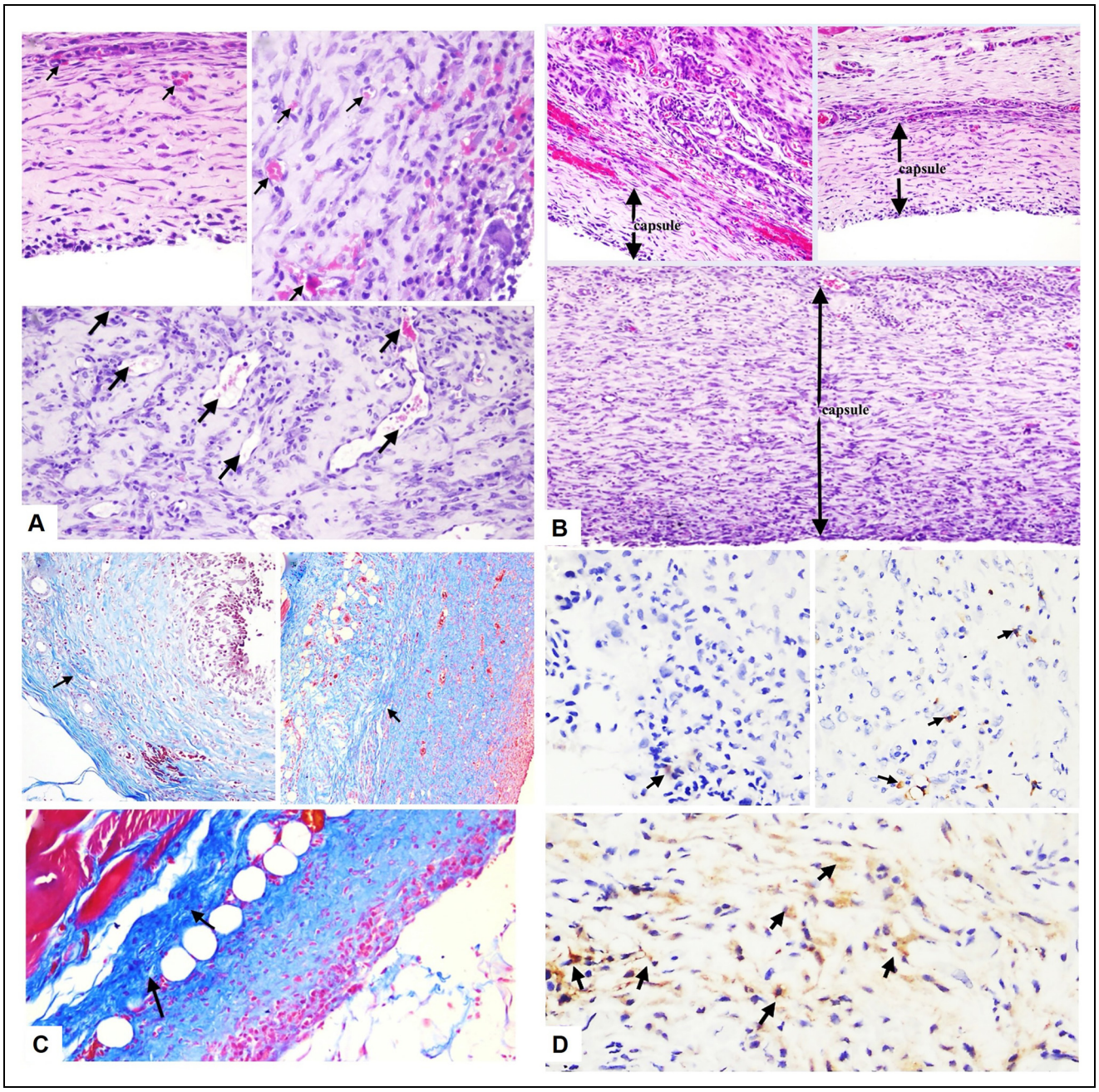


Figure 6. (A) Assessment of vessel density in the capsule between groups (vessels are shown by arrows). (B) Measurement of capsule thicknesses. (C) Fibrosis in the capsule. As collagen accumulation and maturation increase, the color becomes darker (arrows indicate collagen deposition). (D) Sections stained with anti-CD68 showing histiocytes (arrowed) in representative tissue samples from the 3 groups. Group 1, a low concentration of histiocytes seen; Group 2, a moderate density of histiocytes present; Group 3, the highest density of histiocyte infiltration was found in this group (CD68, 400 × magnification), respectively.

week. Fibroblasts synthesize type 1 collagen. At the end of the second week, cytokines that inhibit this pathway are activated with the effect of increasing the amount of collagen at the site of healing, and fibroblast proliferation decreases.[21] As the collagen matures in the capsule tissue, fibroblast numbers decrease and they are replaced by fibrocytes, with an increase in fibrosis in the capsule tissue and the capsule thickens.[22] In the present study, although fibrosis was more marked in Group 3 in which the tissue expanders were inflated excessively and infrequently in each session, fibroblasts were less evident. In addition, while the fibroblast density was similar in Groups 1 and 2, Group 2 exhibited greater fibrosis. Capsular fibrosis is affected by many factors other than just fibroblast number and action. In the wound healing and fibrosis cascade cells, such as histiocytes, pericytes, and epithelial and endothelial cells as well as fibroblasts are involved.[21]

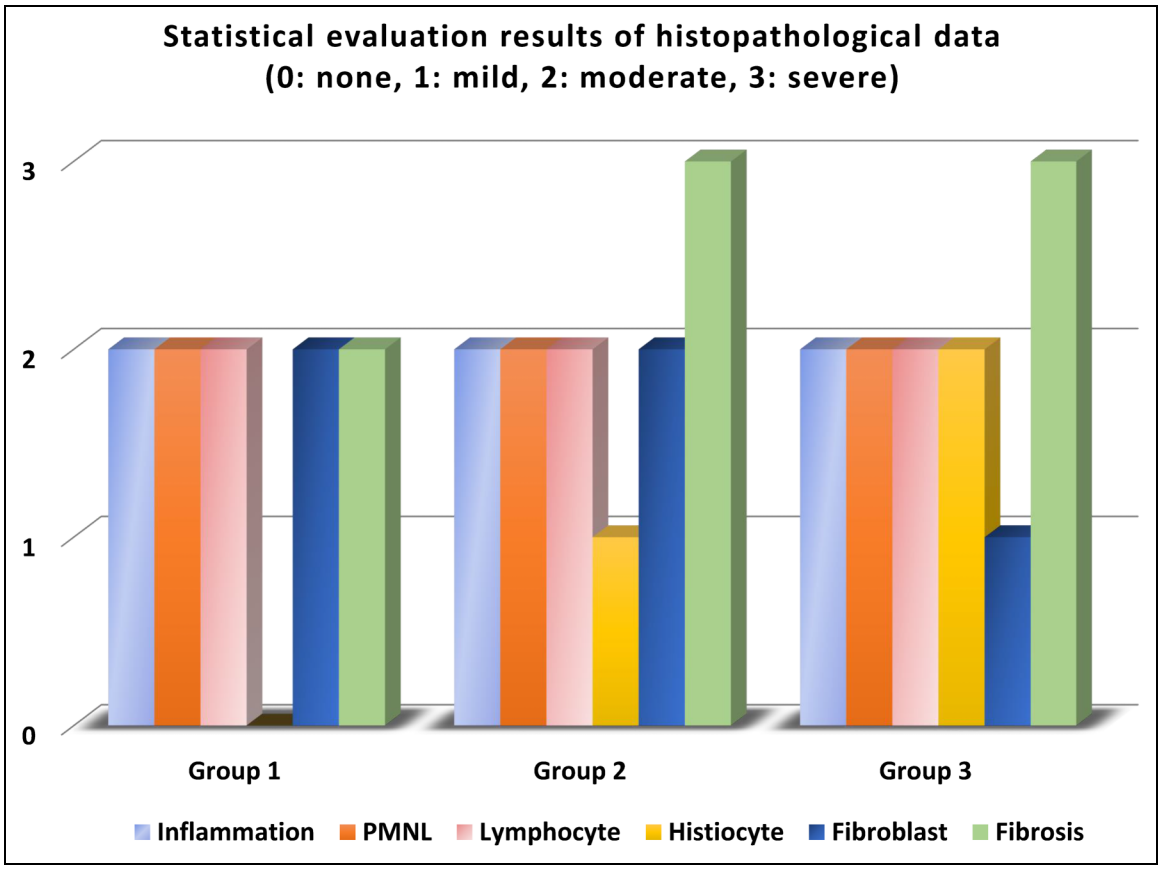


Figure 7. Statistical evaluation results of histopathological data (0: none, 1: mild, 2: moderate, and 3: severe).

In addition, there is a complex milieu of cytokines and chemokines, including transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), and interleukins 1 and 6, all interacting with each other and the cellular components.[21,23] In recent years, it has been shown that hematopoietic cells and, to a lesser degree, epithelial and endothelial cells all contribute to collagen production in various fibrotic diseases.[24] Therefore, although the fibroblast is the main cell responsible for capsule formation, many other mechanisms may also affect capsular fibrosis.

Histiocytes are the types of macrophages found in connective tissues. This cell type is responsible for reacting to the presence of foreign bodies.[25] In the present study, Group 1 exhibited the least capsule thickness and the lowest scores for fibrosis. In addition, there was scant evidence of histiocyte infiltration in tissue samples from this group. While the level of fibrosis was similar in Groups 2 and 3, histiocyte infiltration was more pronounced in Group 3. The statistical significance of this difference indicates that histiocyte also plays a role in the fibrosis mechanism.[26] Histiocytes produce growth factors and cytokines stimulating fibroblasts. Histiocytes stimulate fibroblast activation in the early stages of capsular contracture development and over time, collagen deposition in the capsule becomes predominant and progresses to significant scarring with fibrosis and symptomatic contracture.[26,27] For this reason, one area of research that deserves greater consideration is the inhibition of histiocyte infiltration or inhibition of action once in situ in the wound site.

The mechanical stress that occurs in the soft tissues with the inflation of the tissue expander initiates cellular proliferation and tissue regeneration and increases neovascularization.[28] In the present study, different mechanical stresses were applied to the skin flap per unit of time by inflating tissue expanders with different frequencies and volumes (Group 1 received 1 cc of saline daily, Group 2 received 3 cc of saline every 3 days, and Group 3 received 10 cc of saline every ten days.) Accordingly, even if the fluid volumes in the expander were the same on some days, it was thought that since this volume was achieved gradually in Group 1, the mechanical effect at that moment (and the response of the cells to this effect) would be different from Group 3 which achieved this effect suddenly. The mechanical stress created by the tissue expander per unit time was the highest in Group 3 and also the number of vessels was also the highest in this group with the opposite seen in Group 1.

In the present study, inflating the tissue expander with a small volume at frequent intervals in Group 1 reduced capsule thickness and no histiocyte infiltration was seen. However, the resulting flap surface area was the smallest, although not significantly smaller than in Group 2 or 3.

Table 2. The Capsule Biopsies Were Evaluated and Scored Histopathologically Following the Tissue Expansion Protocol.

		Capsule thickness (μm)	Inflammation score	PMNL count score	Lymphocyte count score	Histiocyte count score	Fibroblast count score	Fibrosis	Number of vessels
Group 1	1. rat	400	2	2	2	0	2	2	45
	2. rat	1000	2	2	2	0	2	2	80
	3. rat	520	2	1	2	1	1	3	70
	4. rat	600	1	1	1	0	1	3	25
	5. rat	1200	2	2	2	1	3	2	165
	Median	600	2	2	2	0	2	2	70
Group 2	1. rat	420	1	1	1	1	1	3	100
	2. rat	1000	2	2	2	1	2	3	85
	3. rat	1000	2	2	1	0	2	2	90
	4. rat	900	3	3	2	1	2	2	65
	5. rat	1100	3	3	2	1	3	3	180
	Median	1000	2	2	2	1	2	3	90
Group 3	1. rat	700	2	2	2	2	1	3	110
	2. rat	1000	2	2	2	3	1	3	100
	3. rat	720	2	2	2	1	2	2	95
	4. rat	1000	2	2	2	3	2	3	40
	5. rat	300	1	1	1	1	1	3	30
	Median	720	2	2	2	2	1	3	95
P value		.681	.502	.360	.727	.025*	.392	.459	.505

Abbreviation: PMNL, polymorphonuclear leucocytes.
Statistical analysis was performed based on the Kruskall-Wallis test (*: Histiocyte density is $P < .05$, statistically significant).

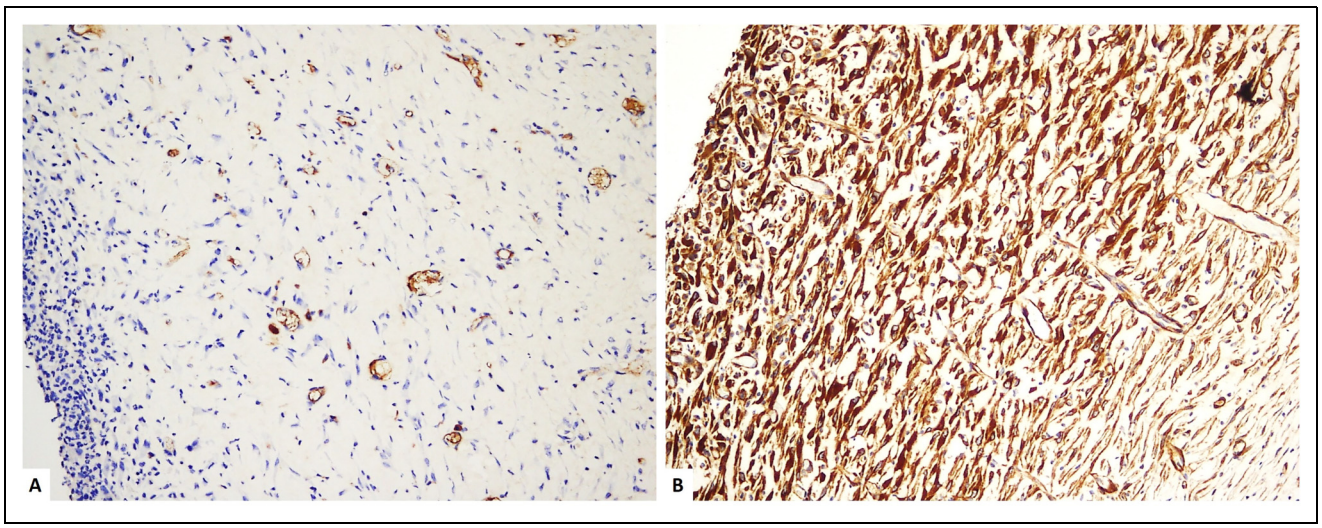


Figure 8. (A) Smooth muscle actin (SMA) staining pattern in vascular structures within rat capsule tissue. (B) SMA staining pattern in both vascular walls and fibroblasts, which enhances the contractile activity of rat subcutaneous fibroblasts (SMA, 200 × and 400 × magnification).

Group 1 also exhibited the least neovascularization, suggesting a slower and more prolonged healing process. In clinical practice, calling patients to the hospital frequently for inflation can be difficult both socially and financially. This is why, in suitable patients, it is recommended to use the inflation interval applied in Group 3, where capsule thickness is acceptable but skin flap gain is high. By using this technique, both more skin flaps and patient comfort can be achieved by inflating the tissue expander to the level deemed appropriate by the skin flap circulation and the patient's pain threshold. However, it may be more beneficial to inflate the tissue expander a small amount at more frequent intervals, while sacrificing some skin flap gain in patients who are prone to fibrosis or are predicted to have increased capsule thickness due to the effect of radiotherapy and chemotherapy, such as in patients undergoing breast reconstruction.

This study has several limitations. Firstly, the use of a rat model, while useful for initial assessments, may not fully replicate the complexities of human tissue expansion and healing

processes. Differences in skin anatomy, wound healing rates, and metabolism between rats and humans may impact the generalizability of the findings. Additionally, the relatively short duration of the study may not capture the long-term effects of different inflation protocols on capsule formation and flap integrity. Variability in individual responses to mechanical stress and pharmacological interventions was not accounted for, which could influence the outcomes. Further research with longer follow-up periods and larger sample sizes in more clinically relevant models is necessary to validate these results and translate them effectively to human applications.[29] Although the rat model is not a perfect model for tissue expansion, it allows the formation of a capsule around the tissue expander in a short time due to rapid wound healing.

Conclusions

This study explored how varying tissue expander inflation protocols—different volumes and frequencies—affect flap formation, tissue healing, scarring, and vascularization. The most frequent, lowest volume inflation resulted in a smaller flap area but improved tissue health parameters, except for neovascularization. This protocol may be advantageous for patients at risk of increased capsule thickness due to radiotherapy, chemotherapy, or those prone to fibrosis. Conversely, for patients where flap size is critical, less frequent inflations with larger volumes may be more appropriate to maximize flap size and minimize capsule thickness. Further research is needed to refine these protocols for optimal clinical outcomes.

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Author Contributions

BDC, CID, EKY, IT, MSA, and BYB collected the data and drafted the manuscript. BDC, CID, EKY, and BYB edited the manuscript, and participated in the study design and coordination. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this published article.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

All procedures performed in the study were conducted in accordance with the guidelines outlined in the Helsinki Declaration and its amendments. The study protocol was approved by the Animal Research Ethical Committee of Kocaeli University (Project No: 2021/01).

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Supplemental Material

Supplemental material for this article is available online.

References

1. Argenta LC. MMW. Mathes plastic surgery volume 1 general principles. In: SJ Mathes ed., *Mathes plastic surgery volume 1 general principles*. 2nd ed.; Saunders Elsevier; 2006:539–567.
2. Bassetto F, Pandis L, Azzena GP, et al. Complete implant wrapping with porcine-derived acellular dermal matrix for the treatment of capsular contracture in breast reconstruction: A case-control study. *Aesthetic Plast Surg*. 2022;46(4):1575–1584. doi: 10.1007/s00266-022-02826-6
3. Adams WP. Capsular contracture: What is it? What causes it? How can it be prevented and managed? *Clin Plast Surg*. 2009;36(1):119–126. doi: 10.1016/j.cps.2008.08.007
4. Copcu E, Sivrioglu N, Sisman N, Aktas A, Oztan Y. Enhancement of tissue expansion by calcium channel blocker: A preliminary study. *World J Surg Oncol*. 2003;1(1):1–9. doi: 10.1186/1477-7819-1-19
5. Guimier E, Carson L, David B, Lambert JM, Heery E, Malcolm RK. Pharmacological approaches for the prevention of breast implant capsular contracture. *J Surg Res*. 2022;280:129–150. doi: 10.1016/j.jss.2022.06.073
6. Irkoren S, Ozkan HS, Ceylan E, Sivrioglu N, Tataroglu C, Durum Y. The effect of Botox on the implant stabilization and capsular formation: An experimental study. *Ann Plast Surg*. 2015;75(1):91–97. doi: 10.1097/SAP.0000000000000005
7. Paşca A, Bonci EA, Chiuzan C, et al. Treatment and prevention of periprosthetic capsular contracture in breast surgery with prosthesis using leukotriene receptor antagonists: A meta-analysis. *Aesthetic Surg J*. 2022;42(5):483–494. doi: 10.1093/asj/sjab355
8. Moreira M, Fagundes DJ, Simões MJ, Taha MO, Perez LMN, Bazotte RB. The effect of liposome-delivered prednisolone on collagen density, myofibroblasts, and fibrous capsule thickness around silicone breast implants in rats. *Wound Repair Regen*. 2010;18(4):417–425. doi: 10.1111/j.1524-475X.2010.00601.x

9. Wang X, Zhang J, Chen W, et al. Study on the effects of estradiol in *Staphylococcus epidermidis* device-related capsule formation. *Aesthetic Plast Surg*. 2019;44(2):558–569. doi: 10.1007/s00266-019-01567-3
10. Klopfleisch R. Multiparametric and semiquantitative scoring systems for the evaluation of mouse model histopathology – A systematic review. *BMC Vet Res*. 2013;9:123. doi: 10.1186/1746-6148-9-123
11. Bui JM, Perry T, Ren CD, Nofrey B, Teitelbaum S, Van Epps DE. Histological characterization of human breast implant capsules. *Aesth Plast Surg*. 2015;39:306–315. doi:10.1007/s00266-014-0439-7
12. Zimman OA, Toblli J, Stella I, Ferder M, Ferder L, Inserra F. The effects of angiotensin-converting-enzyme inhibitors on the fibrous envelope around mammary implants. *Plast Reconstr Surg*. 2007;120(7):2025–2033. doi: 10.1097/01.prs.0000287381.93729.e2
13. Bachour Y, Bargon CA, de Blok CJM, Ket JCF, Ritt MJPF, Niessen FB. Risk factors for developing capsular contracture in women after breast implant surgery: A systematic review of the literature. *J Plast Reconstr Aesthetic Surg*. 2018;71(9):e29–e48. doi: 10.1016/j.bjps.2018.05.022
14. Kyle DJT, Oikonomou A, Hill E, Bayat A. Development and functional evaluation of biomimetic silicone surfaces with hierarchical micro/nano-topographical features demonstrates favourable in vitro foreign body response of breast-derived fibroblasts. *Biomaterials*. 2015;52(1):88–102. doi: 10.1016/j.biomaterials.2015.02.003
15. Ramos-Gallardo G, Cuenca-Pardo J, Rodríguez-Olivares E, et al. Breast implant and anaplastic large cell lymphoma meta-analysis. *J Investig Surg*. 2017;30(1):56–65. doi: 10.1080/08941939.2016.1215576
16. Veras-Castillo ER, Cardenas-Camarena L, Lyra-Gonzalez I, et al. Controlled clinical trial with pirfenidone in the treatment of breast capsular contracture: Association of TGF-β polymorphisms. *Ann Plast Surg*. 2013;70(1):16–22. doi: 10.1097/SAP.0b013e31822284f4
17. Hwang K, Sim HB, Huan F, Kim DJ. Myofibroblasts and capsular tissue tension in breast capsular contracture. *Aesthetic Plast Surg*. 2010;34(6):716–721. doi: 10.1007/s00266-010-9532-8
18. Yu Q, Sheng L, Yang M, Zhu M, Huang X, Li Q. Tanshinon IIA injection accelerates tissue expansion by reducing the formation of the fibrous capsule. *PLoS One*. 2014;9(8):e105756. doi: 10.1371/journal.pone.0105756
19. Joseph J, Squier C, Bardach J. The effects of theophylline and papaverine in enhancing skin expansion in Guinea pigs. *Eur J Plast Surg*. 1988;11(2):60–64. doi: 10.1007/BF00299211
20. Tang Y, Luaii J, Zhang X. Accelerating tissue expansion by application of topical papaverine cream. *Plast Reconstr Surg*. 2004;114(5):1166–1169. doi: 10.1097/01.prs.0000135854.48570.76
21. Broughton G, Janis JE, Attinger CE. The basic science of wound healing. *Plast Reconstr Surg*. 2006;117(7 SUPPL.):12S–34S. doi: 10.1097/01.prs.0000225430.42531.c2
22. Pilling D, Vakil V, Cox N, Gomer RH. TNF-α-stimulated fibroblasts secrete lumican to promote fibrocyte differentiation. *Proc Natl Acad Sci U S A*. 2015;112(38):11929–11934. doi: 10.1073/pnas.1507387112
23. Weiskirchen R, Weiskirchen S, Tacke F. Organ and tissue fibrosis: Molecular signals, cellular mechanisms and translational implications. *Mol Aspects Med*. 2019;65:2–15. doi: 10.1016/j.mam.2018.06.003
24. Mack M. Inflammation and fibrosis. *Matrix Biol*. 2018;68-69:106–121. doi: 10.1016/j.matbio.2017.11.010
25. Sheikh Z, Brooks PJ, Barzilay O, Fine N, Glogauer M, Stampfl J. Macrophages, foreign body giant cells and their response to implantable biomaterials. *Materials (Basel)*. 2015;8:5671–5701. doi: 10.3390/ma8095269
26. Siggelkow W, Faridi A, Spiritus K, Klinge U, Rath W, Klosterhalfen B. Histological analysis of silicone breast implant capsules and correlation with capsular contracture. *Biomaterials*. 2003;24(6):1101–1109. doi: 10.1016/s0142-9612(02)00429-5
27. Kamel M, Protzner K, Fornasier V, Peters W, Smith DI D. The peri-implant breast capsule: An immunophenotypic study of capsules taken at explantation surgery. *J Biomed Mater Res*. 2001;58:88–96. doi: 10.1002/1097-4636(2001)58:1<88::aid-jbm130>3.0.co;2-7
28. Erba P, Miele LF, Adini A, et al. A morphometric study of mechanotransductively induced dermal neovascularization. *Plast Reconstr Surg*. 2011;128(4):288e–299e. doi: 10.1097/PRS.0b013e3182268b19
29. Dorsett-Martin WA. Rat models of skin wound healing: A review. *Wound Repair Regen*. 2004;12(6):591–599. doi: 10.1111/j.1067-1927.2004.12601.x