

# Methods of Fat Tissue Processing for Human Vocal Fold Injection: A Systematic Review

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**Summary: Objectives.** We analyzed different methods used to process autologous fat tissues for vocal fold injection (VFI). VFI is a safe procedure that preserves the folds' original elasticity and vibration properties and rarely triggers foreign-body reactions, but is often a temporary treatment due to fat reabsorption. To avoid it, selecting a technique that provides as many viable implantable adipocytes as possible is mandatory.

**Study Design.** This is a systematic review.

**Methods.** Data were collected from PubMed, Embase, Ovid, and Cochrane Library. Authors systematically reviewed databases for papers on autologous fat tissue processing methods involving human injections in vocal folds and vocalization outcomes that evolved the acoustic analysis of the voice before and after the surgical procedure, independently of the follow-up time.

**Results.** Nine out of the 517 articles met selection criteria for analysis. No standardized technique was found.

**Conclusion.** There is no standardized technique for processing fat tissue for vocal fold injection. Further research is needed to point out the best available technique.

**Key Words:** Vocal fold–Autologous fat tissue–Processing methods–Voice–Injection laryngoplasty.

## INTRODUCTION

Several articles described many materials to be injected into the human vocal fold in cases of glottic insufficiency. Brunnings was the first to describe such attempt using paraffin injections, in 1911. Several methods came out after the initial study, using materials such as silicone and Teflon, trying to restore the glottic function with minimally invasive interventions.<sup>1</sup> These grafts, however, can trigger an intense inflammatory reaction, which sometimes leads to granuloma formation, and may be reabsorbed or rejected to different degrees. For those reasons, new materials are being developed, and several autologous grafts have been described and tested in animal models.<sup>2–4</sup>

Autologous bioimplants, especially autologous fat tissue (AFT), deserve attention for various reasons: it is rapidly obtained, with low costs, and presents a small risk to stimulate inflammatory reactions; additionally, its viscosity is similar to that of the lamina propria of the vocal fold.<sup>5–8</sup> The use of AFT has been associated with adequate improvement of the voice and laryngeal function.<sup>8,9</sup> However, the techniques employed for processing harvested tissue, as well as the volume to be injected, can alter the quantity of viable adipocytes and graft absorption.<sup>4</sup>

There is still some controversy over the use of fat tissue, for not much is known about the lastingness of the graft, its resorption rate, and its effectiveness on the functional recovery of the larynx.<sup>7,8</sup>

Aware of that gap, the authors of the present study systematically reviewed the literature regarding the use of fat tissue in human vocal folds. Additionally, we intended to find techniques for processing fat tissue that minimize tissular damage

and optimize its application and graft durability, leading to a better vocal quality.

## OBJECTIVES

This study aimed to evaluate the methods for processing AFT to be injected in human vocal folds and correlate it to phonation function.

## MATERIALS AND METHODS

For this systematic review, we followed the norms of the Cochrane Collaboration. Authors considered the method of fat tissue injection in human vocal folds as the “intervention,” and the quality of voice (preoperative and postoperative) was taken as “clinical outcome.” The literature research started on August 8, 2014, and was updated on September 2, 2015.

The authors searched the following terms in medical databases (namely PubMed, Embase, Ovid, and Cochrane Library [<http://onlinelibrary.wiley.com/cochranelibrary/search>]): (*Fats, Subcutaneous* or *Subcutaneous Fats* or *Adipose Tissue, Subcutaneous* or *Fat, Subcutaneous* or *Subcutaneous Adipose Tissue*) and (*Cord, Vocal* or *Cords, Vocal* or *Vocal Cord* or *Vocal Fold* or *Fold, Vocal* or *Folds, Vocal* or *Vocal Folds* or *Vocal Ligament* or *Ligament, Vocal* or *Ligaments, Vocal* or *Vocal Ligaments*). No searching filters were applied.

To search the Literatura Latino-Americana e do Caribe em Ciências da Saúde database, we used the following strategy: MH vocal cords or MH pliegue vocales or MH prega vocal and MH Autoenxerto or Autotransplante or Transplantação Autóloga or Enxerto Autólogo.

We also searched Google, using the Medical Subject Headings terms, to find texts or papers considered “cinereous.”

## Inclusion criteria

The authors selected every study published in English or Latin languages that described the processing techniques of the fat tissue to be injected in human vocal folds and included the acoustic

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analysis of the voice before and after the surgical procedure, independently of the follow-up time.

### Exclusion criteria

We excluded experimental and histological studies and studies that used heterologous grafts or any autologous graft different from fat. We also excluded manuscripts with no description of the methodology or of the surgical technique employed. Studies that described the use of fat tissue in other parts of the body other than the vocal fold were also excluded.

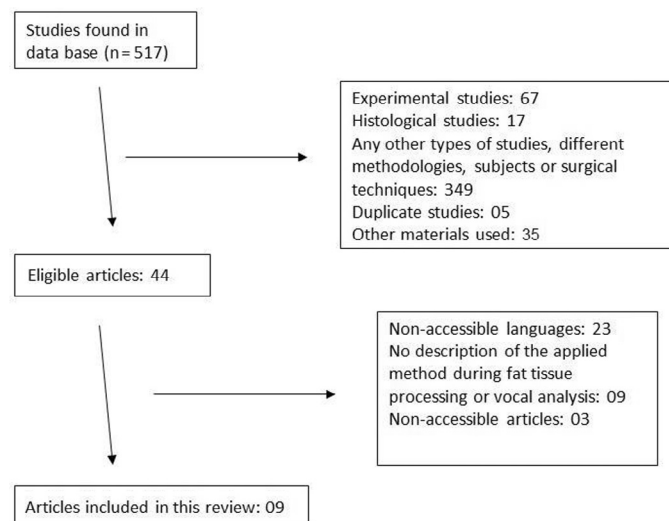
Our initial findings included 517 studies that were reviewed by three different researchers (Figure 1). After the consensus meeting, eligible articles were subjected once more to a review-and-exclusion process (Table 1). Articles not published in English or Latin languages were also excluded. The search resulted in three articles that were eligible for analysis, but only the abstracts were available, and e-mail contact with the corresponding authors was not fruitful. The studies with no description of the fat tissue removal or processing techniques, or with no postsurgical voice analysis were excluded.

Nine articles remained in this systematic review, which were included in the present study and are described in Table 2.

## RESULTS

The nine studies included on this systematic review present processes of obtaining and preparing fat tissue, as described in Table 2. After analyzing the fat tissue processing, clinical outcomes were addressed, namely the acoustic and aerodynamics analysis, before and after the fat injection. The most often used vocal analysis parameters were fundamental voice frequency (in Hertz—Hz), jitter and shimmer parameters (in decibels—dB), maximum phonation time (MPT, in seconds), and the harmonics-to-noise ratio (in decibels). It was not possible to perform a meta-analysis of those parameters because of differences of units used in each of the articles.

Sataloff et al<sup>45</sup> studied four cases of patients with vocal fold scars who underwent the fat injection procedure. In these cases,



**FIGURE 1.** Diagram of the included and excluded studies in this systematic review.

**TABLE 1.**  
**Excluded Articles**

Articles in Nontranslated Languages (n = 23)	Excluded Articles With no Description of the Method or Vocal Analysis (n = 9)
Shvero <sup>10</sup>	Pinto et al <sup>11</sup>
Tamura et al <sup>12</sup>	Hsiung and Pai <sup>13</sup>
Sato et al <sup>14</sup>	Laccourreya et al <sup>15</sup>
Zhang et al <sup>16</sup>	Havas and Priestley <sup>17</sup>
Wen et al <sup>18</sup>	Neuenschwander et al <sup>19</sup>
Sibi and Sram <sup>20</sup>	Umeno et al <sup>21</sup>
Komatsubara et al <sup>22</sup>	Laccourreya et al <sup>23</sup>
Wielgosz and Mroczkowski <sup>24</sup>	Umeno et al <sup>25</sup>
Nishiyama et al <sup>26</sup>	Oluwole et al <sup>27</sup>
Hu et al <sup>28</sup>	
Xu and Han <sup>29</sup>	
Lu <sup>30</sup>	
Sato <sup>31</sup>	
Okamoto et al <sup>32</sup>	
Zheng et al <sup>33</sup>	
Berdal and Hall <sup>34</sup>	
Králík et al <sup>35</sup>	
Neumann <sup>36</sup>	Articles with only abstract available and no answer from author (n = 3)
Ganz <sup>37</sup>	
Gosepath <sup>38</sup>	
Neumann and Treeck <sup>39</sup>	Laccourreya et al <sup>40</sup>
Chládek et al <sup>41</sup>	Bauer et al <sup>42</sup>
Wigand et al <sup>43</sup>	Sataloff et al <sup>44</sup>

the fat tissue was harvested from a nonspecified location in large pieces, washed with saline solution, placed into a Brunnings syringe, and implanted in a tunneled pocket made on the vibratory margin of the vocal folds. The authors described an improvement on voice quality, and the MPT increased from 9.7 to 12 seconds in a 10- to 36-month follow-up. The sustained jitter value improved from 1.195 seconds preoperatively to 0.897 seconds postoperatively.

Shaw et al<sup>46</sup> removed the fat tissue from the left great trochanter area. Small pieces of 2–3 mm were separated from the fibrous tissue and placed into a syringe. Thirty milliliters of saline solution was added, and the entire content was shaken for 3 minutes. The supernatant was removed, and the process was repeated four to six times to get a homogenous fat tissue. The small fat grafts were kept in insulin 100 U/mL for 5 minutes and then drained over a gauze sponge. In cases of vocal fold atrophy, the fat graft was injected into the vocal fold using a Brunnings syringe. In cases of vocal fold palsy, the fat graft was injected into the middle third of the vocal fold in up to four different spots on the thyroarytenoid muscle. The 22 studied patients were divided into two groups (palsy and atrophy of the vocal folds). The shimmer values decreased in both groups postoperatively, from 15.67 dB to 6.34 dB in the palsy group, and from 8.85 dB to 4.31 dB in the atrophy group. There was a 12-month follow-up.

Hsiung et al<sup>47</sup> prepared periumbilical fat tissue, processing samples measuring 2–3 cm and cutting them to 1.0–1.5 mm<sup>2</sup> using a scalpel. The fragments were washed with Ringer lactate

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