Monitoring of Gustatory Stimulation of Salivary Glands by Diffusion-Weighted MR Imaging: Comparison of 1.5T and 3T

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BACKGROUND AND PURPOSE: Our aim was to compare different field strengths monitoring physiologic changes due to oral stimulation of parotid glands by using diffusion-weighted (DW) echo-planar imaging (EPI).

MATERIALS AND METHODS: Twenty-seven healthy volunteers were examined with a DW-EPI sequence at 1.5T and 3T before and after oral stimulation with commercially available lemon juice. The b factors used were 0, 500, and 1000 s/mm². Apparent diffusion coefficient (ADC) maps were evaluated with a manually placed region of interest including the entire parotid gland. For comparison of results, a Student t test was used on the basis of the mean of the volunteer median values. To compare both field strengths, we calculated the Pearson correlation coefficient (r).

RESULTS: DW-EPI MR imaging visualized the parotid glands of all volunteers. With 1.5T, the mean ADC before stimulation was $1.12 \times 10^{-3}$ mm²/s ± $0.08 \times 10^{-3}$ mm²/s. After stimulation with lemon juice, the ADC increased to $1.18 \times 10^{-3}$ mm²/s ± $0.09 \times 10^{-3}$ mm²/s. For 3T, the ADC before stimulation was $1.14 \times 10^{-3}$ mm²/s ± $0.04 \times 10^{-3}$ mm²/s, with an increase to $1.17 \times 10^{-3}$ mm²/s ± $0.05 \times 10^{-3}$ mm²/s after stimulation. For both field strengths, the increase in ADC after stimulation was significant ($P < .001$). High correlations between both field strengths were found pre- and poststimulation ($r = 0.955$, and 0.936, respectively).

CONCLUSION: DW-EPI MR imaging allows monitoring of physiologic changes due to oral stimulation of parotid glands by using DW imaging with high correlation between 1.5T and 3T.
systems. To prevent potential dehydration, there was a 30–45-minute break between the 2 examinations, in which every volunteer drank 250 mL tap water. In volunteers, 1.5T or 3T was alternated as the first examination; thus, 13 volunteers were examined by 1.5T first and 14 volunteers, by 3T first.

The study protocol was approved by the institutional review board, and informed consent was obtained from all volunteers.

**MR Imaging**

We performed 1.5T examinations by using a superconducting system with a 30 mT/m maximal gradient capability and a maximal slew rate of 125 mT/m per millisecond (Magnetom Symphony; Siemens, Erlangen, Germany). The lower part of the circularly polarized (CP) head coil and a standard 2-element CP neck array coil were used. The flexibility of the neck array coil allowed positioning the N1 element (upper part of the coil) right next to the parotid gland. Initially, for anatomic localization of the parotid gland, an axial T1-weighted spin-echo sequence (TR/TE, 500/14 msec) was performed by using a matrix of 192 × 512, FOV of 210 × 280 mm (pixel size, 1.09 × 0.35 mm), a section thickness of 5 mm with an intersection gap of 1.25 mm, and 3 signals averaged. The images extended from the skull base to the section thickness of 5 mm with an intersection gap of 1.85 mm.

Habermann echo sequence (TR/TE, 1500/77 msec) was performed with a matrix of 3 signals averaged. The images extended from the skull base to the section thickness of 5 mm with an intersection gap of 1.25 mm, and 5 sections were acquired. The total acquisition time of this sequence was 2:12 minutes.

For both field strengths, fat suppression was achieved by placing a frequency-selective pulse before the pulse sequence. The b factors used were 0, 500, and 1000 s/mm². These were applied in each of the 3 orthogonal directions to minimize the effects of diffusion anisotropy and were combined to create a trace dataset. ADC maps were generated by using a pixel-by-pixel calculation as referenced by Wang et al (Fig 1A, B). ADC was defined by the following equation: \( \text{ADC} = \left( \frac{\ln(S_{1}/S_{2})}{(b_{2} - b_{1})} \right) \), where \( b_{1} \) and \( b_{2} \) were gradient factors of sequences S1 and S2, and S1 and S2 were signal intensities by the sequences S1 and S2, respectively.

**Image and Data Analysis**

A region of interest enclosing the entire parotid gland was placed on the ADC map, excluding the retromandibular vein (Fig 1). These procedures were performed on all ADC sections of each volunteer where left and right parotid glands were visible pre- and poststimulation. In addition, a circular region of interest containing 100–200 pixels was placed in the CSF next to the spinal cord in every volunteer. All measurements were performed by 2 investigators (C.R.H. and P.G.) in consensus by using the analyzing software MRIRcro (Chris Rorden, University of Nottingham, UK), which lists every pixel intensity of each ADC section in a single region-of-interest output file per volunteer. To minimize potential misplacement due to poor resolution on ADC maps, we validated all regions of interest on axial T1-weighted spin-echo sequences for every single volunteer and region of interest in consensus. We compared the right parotid gland, the left parotid gland, and both glands, pre- and poststimulation. Combined values for both glands were achieved by taking the mean of the separate median values of each gland per volunteer.

All statistical analyses were computed with SPSS 11.5 (SPSS, Chicago, Ill.). For comparison of the results, the Student t test was used, and a 2-tailed P value of less than .05 was determined for statistical significance. To compare both measurement approaches, we calculated the Pearson correlation coefficient (r), and a value of \( r > 0.8 \) was considered to represent a high correlation.

**Results**

In none of the 27 volunteers could pathology be detected either by sonography or by T1-weighted MR images. Consequently, images of all 27 volunteers were included in the analysis. DW-EPI successfully visualized the parotid glands of all volunteers. In none of the volunteers’ skull bases was bone or dental amalgam susceptibility or both observed, and consequently no interference with region-of-interest placements occurred. First, the median ADC values per region of interest and per person were computed. After oral stimulation, an increase of median ADC value was obtained for each measure-
The increase in ADC value after stimulation proved to be significant (P < .001) for the right, left, and both parotid glands. As a reference tissue, the CSF was also measured in all volunteers. The ADC value for CSF was 2.55 × 10⁻³ mm²/s ± 0.2 × 10⁻³ mm²/s at 1.5T and 2.61 × 10⁻³ mm²/s ± 0.3 × 10⁻³ mm²/s by using 3T.

When comparing ADC values achieved by 1.5T and 3T pre- and poststimulation for parotid glands, we computed a high correlation (r = 0.955 and 0.936, respectively) (Fig 4).

**Discussion**

Several studies have shown the possibility of visualizing the parotid glands with DWI. Most of the cited studies dealing with functional MR imaging of salivary glands were conducted with the glands at rest, comparable with the technetium Tc99m pertechnetate uptake, which is described as parenchymal function. The major advantage of salivary gland scintigraphy as the method of choice for functional imaging of the salivary glands is that both parenchymal function and excretory fraction of all major salivary glands can be quantified simultaneously with a single intravenous injection of the radiotracer technetium Tc99m pertechnetate.

Different approaches for evaluating the parotid glands were performed in the few studies published on this topic. Yoshino et al had placed circular regions of interest, which consisted of 100–200 pixels, whereas Sumi et al had included as much of the parotid gland as possible in their regions of interest. In contrast, Patel et al created regions of interest measuring approximately 74 mm² in a relatively homogeneous area in each parotid gland. In an earlier study, we proved that there is no statistically significant difference whether measuring the whole gland or using a region of interest of a certain size, even though we decided to measure the whole parotid gland visible on every section.

The value of DWI of the parotid glands at rest showed a wide variety, ranging from 0.28 × 10⁻³ mm²/s by using an EPI sequence with 2 b factors (b = 500 and 1000 s/mm²) to 1.12 × 10⁻³ mm²/s also by using an EPI sequence with 3 b factors (b = 0, 500, and 1000 s/mm²). Thoeny et al proved that ADC values of the parotid glands calculated from low b values are significantly higher than those calculated from high b val-

**Table 1**: Mean ADC values pre- and poststimulation of parotid glands with commercially available lemon juice using 1.5T*

|          | Right  | Left   | Bilateral |
|----------|--------|--------|-----------|
| Pre-     | 1.14   | 1.11   | 1.12      |
| Post-    | 1.20   | 1.17   | 1.18      |
| Mean     | 1.16   | 1.15   | 1.14      |
| SD       | 0.10   | 0.08   | 0.08      |

*N = 27.

**Table 2**: Mean ADC values pre- and poststimulation of parotid glands with commercially available lemon juice using 3T*

|          | Right  | Left   | Bilateral |
|----------|--------|--------|-----------|
| Pre-     | 1.16   | 1.12   | 1.14      |
| Post-    | 1.19   | 1.15   | 1.17      |
| Mean     | 1.16   | 1.15   | 1.14      |
| SD       | 0.06   | 0.04   | 0.04      |

*N = 27.

For 1.5T, the ADC for the right, the left, and both glands is given in Table 1. For both sides before stimulation, the ADC value was 1.12 × 10⁻³ mm²/s ± 0.08 × 10⁻³ mm²/s (95% confidence interval [CI], 1.09 × 10⁻³ mm²/s to 1.16 × 10⁻³ mm²/s), whereas after stimulation with lemon juice, the ADC value increased to 1.18 × 10⁻³ mm²/s ± 0.09 × 10⁻³ mm²/s (95% CI, 1.15 × 10⁻³ mm²/s to 1.22 × 10⁻³ mm²/s) (Fig 2). The increase in ADC value after stimulation proved to be significant (P < .001) for the right, left, and both parotid glands.

For 3T, the ADC for the right, the left, and both glands is given in Table 2. For both sides before stimulation, the ADC value was 1.14 × 10⁻³ mm²/s ± 0.04 × 10⁻³ mm²/s (95% CI, 1.12 × 10⁻³ mm²/s to 1.16 × 10⁻³ mm²/s), whereas after stimulation with lemon juice, the ADC value increased to 1.17 × 10⁻³ mm²/s ± 0.05 × 10⁻³ mm²/s (95% CI, 1.15 × 10⁻³ mm²/s to 1.19 × 10⁻³ mm²/s) (Fig 3). The increase in ADC value after stimulation proved to be significant (P < .001) for the right, left, and both parotid glands.
ues, assuming that not only true diffusion but also perfusion may contribute to the ADC.

The mean ADC in the present study for parotid glands by using 1.5T and 3T before stimulation was $1.12 \times 10^{-3}$ mm$^2$/s and $1.14 \times 10^{-3}$ mm$^2$/s, respectively. The measured ADC for nonstimulated parotid glands was much higher in our study, in comparison with the cited studies. Sumi et al$^{11}$ reported an ADC value for the parotid gland in a resting state of $0.28 \times 10^{-3}$ mm$^2$/s. In this study, a single-shot spin-echo type of echo-planar MR imaging with a neurovascular array coil was used. The TR was longer (10,000 ms) than that used in our study (1500 ms). Considering this difference, one should have expected a slightly higher ADC in the study by Sumi et al$^{11}$ compared with our results. The mean ADC evaluated by Patel et al$^{12}$ was $0.50 \times 10^{-3}$ mm$^2$/s ± $0.25 \times 10^{-3}$ mm$^2$/s by using DW-EPI. The volunteers in this study had a comparable mean age (39 years versus 31 years). The difference between this and our studies was a single acquisition parameter: the TR used by Patel et al was also longer (10,000 ms) than that used in our study. Unfortunately, Patel et al did not refer to the coil setting and detailed sequence parameters they had used, but showing an SD of almost 50% of the reference value for parotid glands seems to decrease the value of these results. Yoshino et al$^{10}$ presented no ADC values for DW-EPI due to artifacts leading to no analyzable data for this technique.

Thoeny et al$^{14}$ used 4 different b factors in their study (400, 600, 800, and 1000 s/mm$^2$), also dealing with the evaluation of different functional conditions of the parotid glands. For the parotid glands at rest, the mean acquired ADC value was $0.88 \times 10^{-3}$ mm$^2$/s ± $0.09 \times 10^{-3}$ mm$^2$/s. After stimulation with a 500-mg tablet of ascorbic acid, which dissolved after a mean time of 23 minutes, a significant decrease of ADC was measured ($0.81 \times 10^{-3}$ mm$^2$/s ± $0.06 \times 10^{-3}$ mm$^2$/s), followed by a significant increase after 20 minutes ($0.93 \times 10^{-3}$ mm$^2$/s ± $0.1 \times 10^{-3}$ mm$^2$/s). Thoeny et al explained their observations by an emptying of stored saliva in the glands, causing the decrease, followed by an active production of new saliva and an increase of free water in the extra cellular space.$^{14}$ These results are in marked contrast to the presented data in our study; with a significant instantaneous increase of ADC after short-time stimulation with lemon juice for 10 seconds. In contrast, these findings may be explained by an instantaneous increase of free water after stimulation, leading to an increase of ADC within the first 3 minutes. Presenting as well lower ADC values for parotid glands at rest, Thoeny et al reported observations after gustatory stimulation that were completely different from the values observed in the presented study at 1.5T and 3T. At this point, the type of stimulation may have a major impact regarding the different results, which
should be evaluated in a prospective study comparing the different stimulation methods.

It seemed worthwhile for the authors to evaluate different field strengths and different manufacturers to prove the varying data published for 1.5T. The ADC values for the parotid glands at rest by using dual field strength and another manufacturer showed comparable results with the high correlation in our study. Even after oral stimulation, the computed values showed a high correlation, therefore minimizing the possibility of a methodic error in the presented study. Additionally, CSF measurements in the upper area of the neck performed in our study were consistent with the measurements made by other authors, ranging from $2.1 \times 10^{-3}$ mm$^2$/s to $3.36 \times 10^{-3}$ mm$^2$/s. Thus, we can exclude a methodic error in our study, showing an ADC for CSF by using 1.5T and 3T of $2.55 \times 10^{-3}$ mm$^2$/s $\pm$ 0.2 $\times 10^{-3}$ mm$^2$/s and $2.61 \times 10^{-3}$ mm$^2$/s $\pm$ 0.3 $\times 10^{-3}$ mm$^2$/s, respectively.

At first sight, a limitation of the present study is an overlap of the ADC pre- and poststimulation in our population. To establish this technique in a routine clinical setting, one must gain data from a larger population to determine reference values and to gain further experience in patients with pathologic functional changes such as Sjögren syndrome. Nevertheless, the present study is a feasibility one, and its intention was not to present standard values at this time.

Some studies proved possible applications of functional imaging of the parotid gland by using ADC imaging, such as differentiation between recurrent unspecific infections (e.g., sialadenitis or pyogenic parotitis) and the early stages of systemic disorders involving the salivary glands such as sarcoidosis, Sjögren syndrome, or Mikulicz disease. At present, the diagnosis of these important salivary gland diseases still remains difficult with the clinical imaging tests and techniques available. Furthermore, our results offer valuable practical perspectives, which eventually could replace salivary gland scintigraphy as a diagnostic feature in evaluating pathologic functional salivary gland changes. Additionally, DW-EPI might deliver more precise data in regard to monitoring functional gland changes caused by radiation therapy. Perhaps the change of functional conditions can become an additional diagnostic tool differentiating systemic disorders effecting parotid glands. These identifiable changes, in perspective, could facilitate diagnosis of underlying parotid gland disease and, therefore, have a significant impact on further nonoperative or operative treatment.

**Conclusion**

DW-EPI seems to be a reliable noninvasive technique for measuring parotid gland functional changes, representing its excretory function with high correlation between 1.5T and 3T.

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