Ultrasonic Nakagami-parameter characterization of parotid-gland injury following head-and-neck radiotherapy: A feasibility study of late toxicity

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Purpose: The study aims to investigate whether Nakagami parameters—estimated from the statistical distribution of the backscattered ultrasound radio-frequency (RF) signals—could provide a means for quantitative characterization of parotid-gland injury resulting from head-and-neck radiotherapy.

Methods: A preliminary clinical study was conducted with 12 postradiotherapy patients and 12 healthy volunteers. Each participant underwent one ultrasound study in which ultrasound scans were performed in the longitudinal, i.e., vertical orientation on the bilateral parotids. For the 12 patients, the mean radiation dose to the parotid glands was 37.7 ± 9.5 Gy, and the mean follow-up time was 16.3 ± 4.8 months. All enrolled patients experienced grade 1 or 2 late salivary-gland toxicity (RTOG/EORTC morbidity scale). The normal parotid glands served as the control group. The Nakagami-scaling and Nakagami-shape parameters were computed from the RF data to quantify radiation-induced parotid-gland changes.

Results: Significant differences in Nakagami parameters were observed between the normal and postradiotherapy parotid glands. Compared with the control group, the Nakagami-scaling parameter of the postradiotherapy group decreased by 25.8% ($p < 0.001$), and the Nakagami-shape parameter decreased by 31.3% ($p < 0.001$). The area under the receiver operating characteristic curve was 0.85 for the Nakagami-scaling parameter and was 0.95 for the Nakagami-shape parameter, which further demonstrated the diagnostic efficiency of the Nakagami parameters.

Conclusions: Nakagami parameters could be used to quantitatively measure parotid-gland injury following head-and-neck radiotherapy. Moreover, the clinical feasibility was demonstrated and this study provides meaningful preliminary data for future clinical investigation. © 2014 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4862507>]

Key words: ultrasonic tissue characterization, Nakagami imaging, radiation toxicity, parotid gland, xerostomia, head-and-neck cancer

1. INTRODUCTION

The Nakagami distribution is a statistical tool that has been applied in the context of ultrasonic imaging to characterize the biomechanical properties of backscattered radio-frequency (RF) signals from biological tissues. Relatively new, ultrasonic tissue characterization using Nakagami statistics has shown early success in the detection of organ abnormalities, such as those of the breast^{1,2} and liver.³ The purpose of this

study is to evaluate the ability of Nakagami statistics to noninvasively determine and quantify parotid-gland injury following head-and-neck cancer radiotherapy.

Parotid-gland injury is a prevalent side effect suffered by many patients receiving head-and-neck cancer radiotherapy. In the multidisciplinary approach to treating head-and-neck cancer, radiotherapy (RT) plays an essential role in improving locoregional tumor control and overall survival. However, radiotherapy is frequently associated with acute and

chronic complications.⁴ One of the most prevalent and distressing side effects is xerostomia (dry mouth), secondary to radiation-induced parotid-gland injury.⁵ Xerostomia causes pain, difficulty in speech and swallowing, and increased rates of dental caries and oral infection. Although recognized for decades, diagnostic tools to objectively measure radiation-induced parotid-gland injury are still limited in the clinic.

Several imaging studies have been conducted using CT, MRI, MR sialography, PET scintigraphy, and ultrasound to evaluate the severity of salivary-gland injury,^{6–13} each imaging modality shows some degree of success. Volume reduction of parotid glands after radiotherapy has been observed with CT and MRI. MR sialography was proposed as a functional imaging tool to assess the salivary ductal flow. Astrinidou *et al.* demonstrated, in a pilot study of nine patients, that MR sialography can depict radiation-induced changes to the salivary glands and ducts post-RT without the use of any contrast medium or stimulation. Wada *et al.* measured the salivary secretion function response to salivary secretion stimulation in a perspective study of 16 patients before and after head-and-neck cancer RT, and found irradiated salivary gland had strong influence on the clinical severity of xerostomia. Another promising imaging technology is salivary-gland scintigraphy with 99 mTc-pertechnetate. Salivary gland scintigraphy is a PET imaging technique that can provide a detailed functional evaluation of salivation as it measures the amount and speed of radioisotope uptake and excretion of the major glands. Buus *et al.* showed individual radiation response of parotid glands using dynamic PET. In recent years, several groups have reported ultrasound studies on radiation-induced parotid-gland injury. In conventional B-mode studies, increased heterogeneity was reported in the post-RT parotid glands.¹⁴ In the Doppler study of late toxicity in parotid glands, significant differences were demonstrated in the high peak systolic velocity, resistive index, and pulsatility between postirradiation and healthy parotid glands.^{7,15} Compared with CT, MR, MR sialography, and PET scintigraphy, ultrasound imaging of the parotid glands has its unique advantages, such as being the safest (nonradiation), fastest (5–10 min scan) and most cost-effective imaging modality.

Recently, our group conducted a series of ultrasound studies to explore statistical methods of quantitatively characterizing ultrasound images of parotid glands. Based on B-mode images, we demonstrated that first-order statistical features derived from the echo histogram¹⁶ and second-order statistical texture features based on the gray level co-occurrence matrix (GLCM) could provide quantitative measures of post-radiotherapy parotid injury.¹⁷ Herein, we describe our current efforts in developing a Nakagami method based on analysis of the backscattered RF signals. Similar to previous B-mode based statistical methods, the Nakagami method provides quantitative measures of parotid changes induced by radiation. Distinct from the B-mode based methods, the Nakagami approach reveals the biomechanical properties of tissue microstructures, such as the arrangement and concentration of scatterers. In addition, Nakagami parameters are less dependent on system parameters, such as dynamic range and time-gain compensation.¹⁸

We have conducted a clinical study to test the feasibility of using Nakagami parameters to detect radiation-induced parotid-gland injury. This paper describes ultrasound examination of the parotid glands, summarizes the Nakagami statistical model, details the data processing procedures, and then presents the Nakagami parameter results of post-RT parotid glands. The Nakagami parameters of post-RT parotid glands were compared with a group of healthy controls.

2. MATERIALS AND METHODS

2.A. Patient population and treatment

Between January 2011 and March 2012, we enrolled 24 participants (including 12 healthy volunteers and 12 patients post-RT for head-and-neck malignancies). Our institutional review board approved this study, and written informed consent was obtained from all participants. The eligibility criteria for both healthy volunteers include: (1) Participants must be ≥ 18 years of age. (2) No prior radiotherapy to the head and neck or surgery to the head and neck for any reason. (3) No prior malignancies or chemotherapy. (4) No salivary gland malignancy. (5) No salivary gland disease, e.g., Sjögren's syndrome. The eligibility criteria for the post-RT patients include: (1) Participants must be ≥ 18 years of age; (2) Biopsy-confirmed histological diagnosis of squamous cell carcinoma of the oropharynx, hypopharynx, larynx, or patients with unknown primary tumor with unilateral metastases to the neck nodes; (3) Radiation volume $\geq 80\%$ of major salivary glands (parotids); (4) No salivary gland malignancy; (5) No salivary gland disease, e.g., Sjögren's syndrome; and (6) Clinically confirmed xerostomia.

All 12 patients developed Grade 1 (mild dry-mouth, eight patients) or Grade 2 (medium dry-mouth, four patients) post-RT xerostomia. Xerostomia was patient-reported and its level was evaluated using the standard RTOG/EORTC grading system. The 12 post-RT patients ranged in age from 41 to 65 years (mean: 55.4 ± 8.6 years). They include ten males and two females with primary tumor sites in the oral cavity (six patients), oropharynx (three patients), larynx (one patient), and nasopharynx (one patient). All patients had previously received RT for their primary tumors and the radiation regions involved the bilateral neck. The cross-sectional study is based on late toxicity, and all patients were scanned between 1 and 2 years post-RT.

Serving as the control group for the study, the healthy subjects (seven males and five females) ranged in age from 27 to 67 years (mean: 51.0 ± 12.0 years). The exclusion criteria for the control group included subjects with a clinical history of salivary gland diseases or head-and-neck cancers. Thus, the concept of using the Nakagami statistical model to evaluate radiation-induced parotid-gland injury was tested with a total of 24 post-RT and 24 normal parotid glands.

2.B. Data acquisition

Each participant underwent one ultrasound study of his/her right and left parotid glands. As described in the previous

report, we established a standardized protocol for ultrasound scanning of the parotid glands.¹⁷ All ultrasound studies were performed using a clinical scanner (SonixTouch, Ultrasonix, British Columbia, Canada) with a linear array transducer (L14-5/38 probe, 128 elements). All ultrasound data were acquired with the same settings: 10 MHz frequency, 1.00 cm focal length, 3 cm depth, 72% gain, and 80-dB dynamic range. The frequency bandwidth of the transducer is 14–5 MHz; its wavelength at 10 MHz is 0.154 mm; and the incident pulse length is around 0.3 mm. The time-gain-compensation (TGC) was set to the maximum value for all depths. All participants were scanned in the upright seated position, and ultrasound scans of the bilateral parotids were performed in the longitudinal (vertical) orientation. During the ultrasound scan, a thin layer of ultrasound gel was used to ensure good coupling between the face and the ultrasound probe. The probe was placed perpendicular to the scan surface with minimal pressure applied to the face.

During the ultrasound examination, B-mode images of the parotid glands and their corresponding RF echo signals were acquired simultaneously. All B-mode images were saved in 8-bit gray scale, with intensity ranging from 0 to 255. Each B-mode image contained 488 (width) $\times$ 356 (depth) pixels, and the image size was 3.8 cm (width) $\times$ 3.0 cm (depth). In this report, all B-mode images and corresponding parameter images were displayed to the depth of 2 cm since the thickness of the parotid gland was less than 1.5 cm. All RF data were acquired at 20 MHz sampling frequency. Each image frame contained 256 scan lines and 784 sample points/line. The Nakagami parameters were generated from the RF signals.

2.C. Data analysis—The Nakagami statistical model

The Nakagami analysis was applied to the envelope of the backscattered RF echo signals. The theoretical framework for Nakagami imaging relates statistical parameters to properties of the examined tissue.^{19–21} The formulation treats the backscattered ultrasound envelope signals as random signals. Our analysis characterizes tissue structures in terms of a stochastic probability distribution function (PDF) under the Nakagami statistical model. The PDFs of the ultrasonic backscattered envelope X under the Nakagami statistical model are given by

$$f(x) = \frac{2u^u}{\Gamma(u)\omega^u} x^{2u-1} \exp\left(-\frac{u}{\omega}x^2\right) \cdot W(x), \quad (1)$$

where $\Gamma(\cdot)$ is the gamma function and $W(\cdot)$ is the step function.

The Nakagami distribution has two parameters: a scaling parameter and a shape parameter. Let $E(\cdot)$ denote the statistical mean. The Nakagami scaling parameter ω is obtained from the following equation:

$$\omega = E(X^2). \quad (2)$$

The Nakagami shape parameter u is estimated from the second and fourth moments of the backscattered envelopes. The

Nakagami shape parameter u is obtained from the following equation:

$$u = \frac{E^2[X^2]}{E[X^2 - E^2(X^2)]^2}. \quad (3)$$

The Nakagami u is a shape parameter for the PDF. When $u = 1$, the Nakagami distribution reduces to a Rayleigh distribution. When $0 \leq u < 1$, the envelope distribution is considered to be pre-Rayleigh. When $u > 1$, the distribution conforms to post-Rayleigh. This property makes the Nakagami distribution a general model for ultrasonic backscattering.

When the region of interest (ROI) contains randomly located scatterers with varying scattering cross sections, the envelope statistics are likely to be pre-Rayleigh, and Nakagami-shape parameter u is typically between 0.5 and 1.²² Similarly, when some spatial periodicity exists among the scatterers within the resolution cell, then the envelope statistics are post-Rayleigh, and u becomes larger than unity.²³ Typically, u is used as a means to quantify the effective number of scatterers in the resolution cell. This interpretation can be obtained by noting that the random variable $Y = X^2$ follows a gamma distribution, and interpreting the physical relationships between u and the effective number obtained from the gamma distribution.²⁴

We have developed Nakagami statistical analysis procedures to quantitatively characterize the parotid glands. The procedures were carried out through an in-house MATLAB® (Mathworks, Inc., Natick, MA) software routine; Fig. 1 is a diagram showing the sequence of operations in our method.

- Step 1: The first step is a B-mode display either from the saved B-mode image file or a digital reconstruction of the B-mode image from the RF data. The B-mode image serves to identify the overall anatomic structures and guides the ROI selection.
- Step 2: The second step is to determine the ROI for the Nakagami analysis. The ROI could either be fixed or chosen by physicians based on their clinical judgment and need. In this proof of principle study, we used a fixed ROI, which is the region of the entire parotid gland contoured. For future studies, physicians could identify an

FIG. 1. Diagram showing Nakagami parameter characterization procedures.

ROI, e.g., in the high radiation dose region where radiation damages are expected. We note that the accuracy of the parotid-gland Nakagami imaging depends on the accuracy of parotid-gland contour. In this study, an experienced radiologist (S.T.) contoured all parotid glands on the B-mode images. The radiologist was blinded to the Nakagami-parameter images to eliminate any possible bias. The parotid glands are superficial structures wrapping around the mandibles and are often clear on the ultrasound B-mode images. In an earlier study, we demonstrated the interobserver and intraobserver reliability of manual contouring of the parotid glands.¹⁷

- Step 3: We reconstruct ultrasound envelope images by applying the Hilbert transform to the sampled RF signals. The ultrasonic Nakagami parameter images are generated using a square sliding window to process the envelope signals of the whole 2D ultrasound image. The window size is important in Nakagami parameter calculation and determines the resolution of the Nakagami images. There is a trade-off between the resolution and statistical stability of the Nakagami estimation. A previous study suggested that the appropriate sliding window length should be equal or higher than three times the pulse length of the incident ultrasound. In the context of evaluating parotid-gland injury, the resolution is not a major concern. The challenge presented here was to capture the subtle changes induced by radiation and the statistical stability was crucial. Therefore, we used a relatively larger sliding window size of $1.5 \text{ mm} \times 1.5 \text{ mm}$ (37 samples points by 10 lines) to generate Nakagami parameter images, which is 5 times the pulse length to ensure the statistical stability. The sliding window was moved at 1 pixel/point along the depth. With each sliding window, Nakagami scaling and shape parameters were computed through Eqs. (2) and (3).
- Step 4: We calculate the mean and standard deviation of the Nakagami scaling and shape parameters for the contoured ROI or the parotid gland. The performance of using the Nakagami parameters to discriminate the normal parotids and irradiated parotids were evaluated using the probability value (i.e., p value) calculated from the unpaired t -test.

3. RESULTS

We first present two illustrative cases, one healthy volunteer and one post-RT patient, to show how Nakagami parameters can be employed to assay radiation-induced parotid-gland changes. Figures 2(a) and 2(b) show the ultrasound images of the right and left parotid glands of a 40-year-old healthy volunteer. On the B-mode image, the parotid glands, contoured in dotted yellow lines, are visualized and exhibit homogeneous echo texture. Figures 3(a) and 3(b) show the B-mode images of the right and left parotid glands of a 63-year-old woman postradiotherapy. She received external beam radiation treatment between March and May 2009 for squamous cell carcinoma of the mandibular gingiva. The primary tumor received a total dose of 65.0 Gy. The mean radiation dose delivered to

FIG. 2. Ultrasound images of normal parotid glands (between the dotted yellow lines). The B-mode images of the right parotid gland (a) and the left parotid gland (b) of a 40-year-old healthy volunteer show homogeneous echo texture.

the left parotid gland was 30.6 Gy, and to the right parotid gland was 28.9 Gy. She underwent ultrasound scanning 22 months after treatment completion. At the time of scanning, she was experiencing moderate (grade 2) xerostomia according to the physician's (J.J.B.) clinical assessment. In contrast to the normal parotid glands, the irradiated parotid glands

FIG. 3. Ultrasound images of the irradiated parotid glands (between the dotted yellow lines). The B-mode images of the right parotid gland (a) and the left parotid gland (b) of a 63-year-old woman 22 months post-RT show heterogeneous echo texture.

FIG. 4. Comparison of B-mode image and Nakagami parameter maps of a normal control and a post-RT patient (the parotid glands are between the dotted yellow lines). Left column (normal parotid gland): (a1) B-mode image of the parotid, (a2) Nakagami-scaling image, and (a3) Nakagami-shape image. Right column (post-RT parotid gland): (b1) B-mode image of the parotid, (b2) Nakagami-scaling image, and (b3) Nakagami-shape image. The maximum values of Nakagami scaling and shape parameters were assigned dark red shadings, which changed from blue to red with increasing value. Compared with the control, decreased Nakagami shape and scaling parameter values were observed in the post-RT patient.

revealed heterogeneity on the ultrasound images. Hypoechoic (darker) areas and hyperechoic (brighter) lines or spots are visible on the B-mode images of these parotid glands. The Nakagami-scaling and Nakagami-shape parameter images of the right parotid glands were generated according to the algorithmic procedure described above. The mean Nakagami-scaling parameter values were $(3.18 \pm 0.71) \times 10^8$ for the normal parotid glands, and $(2.36 \pm 0.56) \times 10^8$ for the irradiated parotid glands. The mean Nakagami-shape parameter values were 1.82 ± 0.26 for the normal parotid glands, and 1.25 ± 0.21 for the irradiated parotid glands. As shown in Fig. 4, a pseudocolor scale was applied to clearly reveal the information in the two Nakagami maps. The maximum values of u and ω were assigned a dark red shading, which changed from blue to red with increasing value. Decreases in Nakagami-scaling and Nakagami-shape parameter values of the post-RT can be seen on the Nakagami-shape and Nakagami-scaling maps.

We generated the Nakagami scaling and shape images for all the participants (22 post-RT and 24 normal parotid glands) and calculated the average and the standard deviation of the Nakagami parameters of the parotid glands. Since the well-known study by Eisburch *et al.* reported that a mean dose of 26 Gy or above to the parotid glands resulted in significant decreases in the salivary flow upon stimulation, the mean dose of 26 Gy has been used as the threshold in radiotherapy.²⁵ Accordingly, we excluded two parotid glands which received a mean dose less than 26 Gy. Overall, the mean radiation dose of the 22 parotid glands was 37.7 Gy (range: 27.9–66.0 Gy). The mean follow-up period between the completion of RT and the ultrasound scan was 16.3 months (STD = 4.8 months, range 13.3–23.9 months). Table I shows the Nakagami-scaling and Nakagami-shape parameter values of the normal and post-RT groups. Compared with the control group, the Nakagami-scaling parameter of the post-RT group decreased by 25.8% ($p < 0.001$), and the Nakagami-shape

TABLE I. Nakagami parameters (mean $\pm$ standard deviation) of the control and post-RT groups.

Nakagami parameters	Control group ($n = 24$)	Post-RT group ($n = 22$)	Percentage change	p value
Scaling parameters (10^8)	3.18 ± 0.71	2.36 ± 0.56	–25.8%	<0.001
Shape parameters	1.82 ± 0.26	1.25 ± 0.21	–31.3%	<0.001

FIG. 5. ROC curves of the Nakagami-scaling parameter (a) and Nakagami-shape parameter (b).

parameter decreased by 31.3% ($p < 0.001$). Statistical analyses confirmed significant differences between post-RT and normal parotid glands in both Nakagami parameters.

The predictive discriminatory powers on the parotid gland injury of the two Nakagami parameters were further analyzed with receiver operating characteristic (ROC) curves. The diagnostic accuracy of Nakagami parameters was measured by calculating its sensitivity and specificity, as shown in Fig. 5. For the Nakagami-scaling parameter, the cutoff value in the ROC curves, estimated by maximizing both sensitivity and specificity, was 2.74×10^8 and its area under the ROC curve was 0.81. For the Nakagami-shape parameter, the cutoff value for the Nakagami-shape parameter was 1.57 and the area under the ROC curve was 0.95.

4. DISCUSSION

The use of radiotherapy to treat head-and-neck cancer often involves radiation exposure to the parotid glands, which frequently leads to the debilitating and long-term side effect xerostomia. In this study, we have developed Nakagami-statistical-analysis procedures to evaluate parotid-gland injury associated with head-and-neck cancer radiotherapy. The premise behind our Nakagami-parameter method is that high doses of radiation alter the structural and morphological characteristics of the parotid glands, and that these alterations can cause observable changes in the Nakagami parameters.

Nakagami-scaling and Nakagami-shape parameters, estimated from the statistical distribution of the ultrasonic RF signals backscattered from tissues, were employed as a means for characterizing the biomechanical properties of the parotid glands. In this pilot study of 24 participants, we have demonstrated its clinical efficacy in characterizing radiotherapy-associated parotid-gland injury. Compared with the control group, significant decreases in Nakagami-scaling and Nakagami-shape parameters were observed in irradiated

parotid glands. Histologically, normal parotid glands consist entirely of serous cells—with densely packed translucent secretory granules.^{5,26–29} These densely packed cells and granules provide uniform and highly reflective interfaces for the ultrasound beams,³⁰ accounting for the homogeneous and hyperechoic appearance of the normal parotid glands. Therefore, the Nakagami-scaling parameter, which is the power of the mean envelope intensity, is higher for the normal parotid gland than the irradiated gland. Following head-and-neck radiotherapy, radiation-induced chronic sialadenitis, with inflammatory infiltrate and fibrosis was reported in the irradiated parotid glands.^{27,31–33} Compared with normal tissues, fibrotic tissues are associated with increased sound speed and density, which make the scatterers exhibit a higher degree of variability. Previous studies have shown that fibrotic tissues tend to have the backscattered statistics of pre-Rayleigh distribution.^{3,34} With the higher intensity variation resulting from inflammation and fibrosis, the Nakagami-shape parameter shows a decreasing trend postradiation.

Despite large patient-to-patient variation, the Nakagami parameters were able to detect radiation-induced parotid-gland injury. With an area under the ROC curve of 0.81, the Nakagami-scaling parameter had good diagnostic accuracy in detecting radiation-induced parotid injury. With an area under the ROC of 0.95, the Nakagami-shape parameter had an excellent accuracy in the diagnosis of parotid-gland injury. One of the 12 enrolled patients was a 70-year male with squamous cell carcinoma of the oropharynx. Between November and December 2009, he received 70 Gy to the primary tumor; his right parotid gland received 0 Gy radiation while his left parotid gland received a mean dose of 27.2 Gy. He subsequently developed Grade 1 xerostomia and the parotid glands were scanned with ultrasound during his 1-year follow-up (Fig. 6). Compared with the nonirradiated right parotid gland, the Nakagami-scaling parameter of the irradiated left parotid gland decreased by 22% (right parotid: $\omega = 2.79 \times 10^8$, left

FIG. 6. A 70-year-old patient with squamous cell carcinoma of oropharynx cancer who has received 70 Gy to the primary tumor. The mean dose to the right parotid was 0 Gy and the mean dose to the left parotid gland was 27.2 Gy.

parotid: $\omega = 2.18 \times 10^8$) and the Nakagami-shape parameter of the left parotid gland decreased by 35% (right parotid: $u = 1.70$, left parotid: $u = 1.11$).

The Nakagami statistical analysis method utilizes RF signals obtained from the clinical ultrasound scanner, and this study's findings are consistent with those of previous B-mode based ultrasound studies.^{7,14,15,35,36} We should note that our Nakagami-parameter analysis, B-mode image and Doppler method are in general independent and complementary. B-mode image provides evidence of the anatomical changes and Power Doppler method provides evidence of the blood-vessel abnormalities of the parotid-gland. Yet Nakagami-parameter imaging has several advantages over the conventional B-mode based studies. As described in the theoretical framework,¹⁹ the backscattered ultrasound RF signals depend on the biomechanical properties (arrangement and concentrations) of the tissue microstructures. Nakagami distribution provides a general model that describes the RF signals; therefore Nakagami parameters provide measures of these biomechanical properties. Moreover, Nakagami distribution describes the statistics of ultrasound signals. Nakagami parameters yield more consistent measures that are independent of system factors such as dynamic range and system gain.¹⁸ Furthermore, Nakagami parameters enable extraction of the weak scattering information that may be lost in the conventional B-mode image interpretation.¹⁸ Such subtle changes may be critical in capturing radiation-induced tissue changes.

While this report has addressed parotid-gland toxicity assessment in head-and-neck radiotherapy, the underlying principles and analyses are applicable to assays of other or-

gans, such as the breast and prostate. For future work, we will continue to enroll patients in our clinical study, and we will investigate the correlations between Nakagami-parameter measured parotid injuries with treatment factors (i.e., radiation dose) and clinical endpoints (i.e., patient-reported xerostomia).

5. CONCLUSIONS

Nakagami statistical analysis, which complements conventional B-mode imaging, has the potential of providing key imaging signatures for ultrasonic characterization of radiation-induced changes in the parotid glands. These procedures remove measurement artifacts and provide objective quantitative, statistical descriptions of tissue microstructures. This pilot study demonstrated the clinical feasibility and significant differences in Nakagami-shape and Nakagami-scaling parameters of the parotid glands between healthy volunteers and post-RT groups. Ultrasound Nakagami parameters provide statistical features of the parotid tissues. Nakagami methods may provide a useful metric of parotid-gland injury secondary to radiation that can be further developed into a low-cost tool for normal-tissue assessment following head-and-neck radiotherapy.

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