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Imaging tooth enamel using zero echo time (ZTE) magnetic resonance imaging

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Abstract

In an event where many thousands of people may have been exposed to levels of radiation that are sufficient to cause the acute radiation syndrome, we need technology that can estimate the absorbed dose on an individual basis for triage and meaningful medical decision making. Such dose estimates may be achieved using in vivo electron paramagnetic resonance (EPR) tooth biodosimetry, which measures the number of persistent free radicals that are generated in tooth enamel following irradiation. However, the accuracy of dose estimates may be impacted by individual variations in teeth, especially the amount and distribution of enamel in the inhomogeneous sensitive volume of the resonator used to detect the radicals. In order to study the relationship between interpersonal variations in enamel and EPR-based dose estimates, it is desirable to estimate these parameters nondestructively and without adding radiation to the teeth.

Magnetic Resonance Imaging (MRI) is capable of acquiring structural and biochemical information without imparting additional radiation, which may be beneficial for many EPR dosimetry studies. However, the extremely short T2 relaxation time in tooth structures precludes tooth imaging using conventional MRI methods. Therefore, we used zero echo time (ZTE) MRI to image teeth ex vivo to assess enamel volumes and spatial distributions. Using these data in combination with the data on the distribution of the transverse radio frequency magnetic field from electromagnetic simulations, we then can identify possible sources of variations in radiation-induced signals detectable by EPR. Unlike conventional MRI, ZTE applies spatial encoding gradients during the RF excitation pulse, thereby facilitating signal acquisition almost immediately after excitation, minimizing signal loss from short T2 relaxation times. ZTE successfully provided volumetric measures of tooth enamel that may be related to variations that impact EPR dosimetry and facilitate the development of analytical procedures for individual dose estimates.

Keywords

MRI; ZTE; EPR; HFSS; Biodosimetry; Segmentation

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1. INTRODUCTION

In a major radiation disaster, such as from a terrorist group detonating an improvised nuclear device in a large urban setting or a major nuclear power plant accident, many thousands of people in the proximate geographic region may have been abruptly exposed to levels of radiation that are sufficient to cause the acute radiation syndrome (ARS)—including the potential for death within a few weeks for substantial numbers of victims if not treated. Several agencies of the US federal government, charged with planning and preparedness for dealing with the public response to such disasters, have issued guidelines about medical responses in such circumstances [1,2]. Such guidelines include identifying the need to quickly and effectively screen a large number of people to determine those who have been exposed to radiation levels warranting further evaluation and treatment and triaging others who would not benefit from entering an over-burdened medical system [3,4]. There is basic agreement among experts in the field that such biodosimetric measurements for triaging large numbers of people should be based on measurements specific to each person rather than based solely on environment dosimetry or population-based estimates [1,4,5,6]. While there are some guidelines based on currently approved technologies to carry out biodosimetry, most biodosimetric methods present serious challenges or inadequacies for being able to quickly assess thousands of people in an infrastructure seriously degraded by the disaster [7,8]. New technologies using dosimetry based on electron paramagnetic resonance (EPR) are currently being developed to address the need for rapid, accurate dose estimates that can be carried out nearby the disaster and capable of providing the needed information to be able to triage thousands of people within a few days [9,10]. EPR dosimetry is based on assessing the stable free radicals produced by exposure to ionizing radiation in tooth enamel and in the keratin present in finger- and toe-nails. The most advanced EPR biodosimetric method involves making in vivo measurements of the upper central incisors with about 5–10 minutes of data acquisition. As this technique moves toward providing the data to secure approval as a medical device by the US Food and Drug Administration (FDA), it is important to understand whether and how our estimates of dose are impacted by normal variations in the incisors, including density and volume of enamel, natural contours of the teeth and their position within the mouth. In order to study the relationship between variations in enamel and EPR-based dose estimates, it is desirable to estimate these parameters nondestructively and without adding radiation to the teeth. While micro computed tomography (MicroCT) and analysis of crushed enamel have been used to characterized the depth and volume of enamel and dentin in teeth, it has the potential of adding dose (MicroCT) and being destructive (crushing) and so we turned to magnetic resonance imaging to try to address the important underlying question of the effect of the distribution of enamel on the magnitude of the measured EPR signal. In particular, we performed zero echo time (ZTE) magnetic resonance imaging (MRI) of extracted teeth to characterize the spatial distribution of enamel with respect to the resonator.

Briefly, in this study, we used an L-band EPR tooth dosimetry system, developed at Dartmouth to measure the radiation induced signal (mRIS) in 10 extracted central incisors that were embedded in a mouth model and subjected to serial irradiation as described below. We then performed finite element simulations of the electromagnetic fields generated by the

EPR resonator used to measure these teeth in order to enable calculation of simulated RIS amplitudes (sRIS) for each tooth. Then, we characterized the spatial distribution of tooth enamel for each tooth through novel use of ZTE MRI, and then calculated the correlations between these distributions and the measured and simulated RIS amplitudes across a dose range of interest for assessing people exposed to levels that would result in ARS. The correlation between the simulated RIS amplitudes and the measured RIS amplitudes was calculated to evaluate the impact of non-geometric factors on the measured amplitude.

2. METHODS

2.1 Zero Echo Time (ZTE) MRI Acquisition

The 10 teeth used in this study were selected from a previous large EPR study on serially irradiated teeth. Therefore, mRIS was well characterized for these teeth in our setup. Prior to being embedded in the mouth model used for the EPR measurements, each tooth was examined using ZTE MRI to delineate enamel. Each tooth was anchored in putty, immersed in water and imaged on a 11.75 T Bruker Avance Spectrometer equipped with triple axes gradients (Bruker BioSpin, Billerica, MA). The 3D ZTE imaging parameters were as follows: TR = 2 ms, field-of-view = 25.6 mm × 25.6 mm × 25.6 mm, acquisition matrix = 256×256×256, number of averages = 16. For comparison, ultrashort echo time (UTE) images were acquired with TR = 8 ms, TE = 20 μs and with the identical acquisition matrix.

2.2 MicroCT Acquisition

There is evidence in the literature [11] that MicroCT can be used to characterize the enamel accurately but its use would deposit dose in the enamel, which is not desirable for our purposes. While MicroCT could potentially be performed after EPR dosimetry has been completed, this could prevent future EPR studies of these teeth with adequately characterized doses. Nonetheless, to gain insight on the accuracy of our results from MRI images, we obtained a MicroCT image and ZTE MRI for comparison on a separate incisor tooth that was not included in the study. A GE MicroCT- Locus SP was used to acquire images with a 90 kVp, 80 uA, 720 projections, 4 frames averaged, an exposure time of 3000 ms, resulting in 0.01 mm resolution. The data were then segmented through an identical process as that used for MRI and the enamel volume was quantitated.

2.3 MRI Image processing

MRI images were thresholded to delineate enamel from surrounding water and dentin, and binarized. Next, a seeded region-of-interest was placed in the enamel and a region-growing algorithm was used to obtain segmented enamel using itk-SNAP (www.itksnap.org). The output data were used to generate enamel depth maps and to create a volumetric mesh for each tooth for use in high field electromagnetic finite element simulations using Ansys High Frequency Structure Simulator (HFSS) software (Ansys, Inc., Canonsburg, PA) in addition to quantitating region-specific enamel volumes. In order to import these raw volumetric data into HFSS, the exterior surface was smoothed.

2.4 Electron Paramagnetic Resonance (EPR) Dosimetry

Measured RIS—EPR tooth dosimetry, in its ultimate intended use, will assess dose based on a single set of in vivo measurements of either central incisor in the upper jaw. To simulate these conditions, we created mouth models consisting of four upper incisors with the two central incisors from the same donor. Four incisors are used to ensure that there are neighboring teeth irradiated to the same added dose and to allow the measurement of both central incisors. Five mouth models were used in this study, with measurements made on both central incisors at five dose levels, i.e., the mouth models were measured at 0, 2, 4, 6, and 10 gray (Gy). The radiation dose was applied serially to each mouth model using a bolus material to simulate tissue in the mouth and using a clinical linear accelerator with 6MV photons. (While not reported here, we also measured the teeth of patients during the course of their standard therapy to receive increments of two Gy during total body irradiation, in preparation for bone marrow transplant [12].) Prior to adding any dose and then after delivery of each fraction of dose, the EPR dosimeter acquired 6 sets of 20 three-second scans at continuous wave L-band operating at 1.15 GHz on each central incisor. Medians of these sets of scans were fit with a non-linear least squares model yielding a dose estimate for an individual tooth [13]. Multiple levels of averaging were applied both in pre and post processing to achieve the most accurate measure possible from the existing data. Each tooth was measured four times to produce the mean mRIS for a given tooth. In data reported here, we used the full set of measurements to develop a calibration curve but the mRIS reported below is based on measurements made after 10 Gy had been added.

Simulated RIS—Consistent with theory, previous studies using finite-element simulations with HFSS software have indicated that the geometry of both the surface coil and sampled volume affect the measured RIS [14]. Hence, the simulations used here needed to reflect the dimensions of the detection coil as well as the enamel volume specific to each tooth. The hardware interface of the EPR in vivo tooth spectrometer used to measure the teeth consisted of a rigid resonant surface coil composed of a 1 mm silver wire in a loop shape with a 10 mm outer diameter. The coil was placed upon an upper central incisor as illustrated in Figure 2, effectively fixing the combined geometry of the tooth and coil. This coil produces a radiofrequency magnetic field distribution over the volume. For uniform density tooth enamel, the amplitude of the EPR signal generated by any subvolume of enamel is linearly proportional to the strength of the radiofrequency magnetic field (B_1) that is perpendicular to the static magnetic field within that subvolume [10]. The grayscale image shown in Figure 2 represents the relative perpendicular B_1 strength across the volume of a single tooth's enamel. It should be noted that the dentin layer (represented by the root in this figure) extends into the interior of the enamel-covered surface shown here, so that the enamel of the tooth actually has a gradient of depth from top to bottom of the surface area; it is because of this complex enamel geometry that we need ZTE MRI. The variation in shaded region in Figure 2 illustrates the sensitivity to size and shape as the gradient of the B_1 field maps differentially across different geometries.

3. RESULTS

3.1 Zero Echo Time (ZTE) MRI

Figure 3 shows a ZTE image of a tooth with superior enamel delineation seen on the ZTE image as compared with other MRI acquisition schemes such as UTE due to increased signal from the dentin. This enabled the extraction and characterization of enamel volume and depth as described later. ZTE MRI also revealed features such as dental carries (Fig. 3b) on teeth that appeared normal on visual inspection.

3.2 Volumetric Analyses

Validation of the technique: Enamel observed from ZTE MRI appeared to be similar to that observed in MicroCT (Figure 4). Caries were bright on MRI and hypodense on MicroCT. For the tooth interrogated using both modalities, the total volume of enamel obtained from ZTE MRI was 81.19 mm^3 and that obtained from MicroCT was 81.47 mm^3 . Note that the resolution of the MRI volumetric meshes, i.e., the spatial distribution of enamel (represented by the detail in the contour lines), was lower than the MicroCT, but the overall shape and structure of the enamel was conserved.

The volumetric meshes from the ZTE MRI for the 10 study teeth are entered into the HFSS simulation, permitting simulation of the relative contribution of the enamel to the EPR dose estimates depending on the relationship of the enamel to the sensitive area of the sensor. The left side of Figure 5 displays a standard upper central incisor in its entirety with the enamel crown, dentin, and root – the enamel alone is displayed below it, showing the part of the tooth captured in the MRI image. The numbered teeth in Figure 5 are images of the 10 upper central incisors used in this study, first displaying the labial (front) perspective where the EPR sensor is placed and then the more complex contour of the lingual (back) of the teeth. Note that the teeth are displayed with the incisal (biting) edge up, i.e., upside down since they are mandibular teeth. Teeth are paired by donor (see Table 1). The identification number on each tooth includes an indication of which type of tooth is imaged; using standard US dental numbering, T8 is the right and T9 the left upper central incisor.

These images illustrate the variability among incisors, even within the same donor, as well as revealing the contoured ridges on the front and back and areas of wear (particularly obvious on the back views as openings on the incisal edge where the dentin is exposed) and fillings (see T8-95 front view).

3.3 Correlations Among Measures of Enamel Volume and Dose Estimates

The enamel geometries were imported into HFSS and positioned with respect to the surface coil according to the standard EPR method for placement for in vivo and in vitro measurements. Table 1 below shows the results from the MRI images, both as a summary measure of total volume and then as incorporated into the HFSS simulations of EPR signals if the tooth were exposed to 10 Gy in an terrorist event, comparing that to the measured EPR dose estimates of these teeth and to a physical measurement of the tooth's height made by dental experts. Both the simulated and measured RIS have been converted to gray for comparison. Recall that these teeth had all been measured after a known dose of 10 Gy had

been added, and note that dose can be estimated for teeth at lower doses. The top portion of the table presents the mean values; the bottom presents Pearson correlations (R) among the variables.

The enamel volume was obtained from the MRI images and was characterized as described earlier in Section 3.2. In data on the 10 study teeth, total volume was correlated strongly to the simple physical measurement of the height of the labial surface ($R=.72$, $p<.05$). Total volume was also strongly correlated with the sRIS ($R=.78$, $p<.05$), but not with the mRIS ($R=-.39$, not significant). The former relationship is not unexpected based on the similar sizes of the teeth and resonator. The tooth's physical height showed this same association with sRIS (i.e., strongly correlated) and mRIS (i.e., not correlated). Unexpectedly, the sRIS and mRIS were not correlated with each other.

4. DISCUSSION

ZTE MRI provided excellent enamel-dentin contrast, comparable to MicroCT, which cannot be achieved using conventional MRI or ultrashort echo time imaging. The resultant MRI-generated 3D images of volume of enamel can successfully be used in simulations that match enamel occurring naturally on a tooth to the microwave intensities that can be detected by EPR spectroscopy to estimate dose. This image acquisition is non-destructive physically and does not impart additional radiation dose to teeth. ZTE also revealed structural impurities and other individual signatures of teeth that make it a useful laboratory technique to probe other structural abnormalities that might affect the EPR signal.

Comparing the ZTE MRI quantitated volume of enamel to the more conventional image in MicroCT for a single tooth provided evidence that MRI can give very similar information, without imparting dose, despite the lower resolution. In comparing MRI measures of enamel to physical measurements of teeth (such as the height of the labial surface), the summary measure of the MRI volume was highly correlated with height, which could be much more readily measured in a disaster situation where EPR tooth dosimetry would be needed. This lends strength to the desirability of identifying whether and how variations in enamel impact the EPR signal, using the more rich 3D information provided by MRI imaging, and then identifying more feasible surrogate measures that can be easily accomplished via photos or physical measurements in the field to correct the EPR dose estimates.

The most puzzling finding in this application was the poor correlation between the simulated RIS, based on the MRI image of the tooth's enamel distribution and the resonator's sensitivity, and the measured RIS of the same tooth ($R=-.08$, NS). One likely explanation is that we have underestimated the importance of nearby radiation sensitive materials, most notably including the neighboring teeth and dentin, both of which were physically present when we measured the teeth with EPR but neither of which were simulated in the sRIS. Additional simulations could be performed including the lateral incisors and dentin, and by including these data, a more accurate model of the radiation sensitive material distribution surrounding the surface coil may be input into HFSS. Another explanation is that we may be overestimating the depth and strength of the B1 field in our simulations. When we simulated the front half of the enamel only, the correlation of sRIS (front half only) with mRIS was

0.62 with a p-value of 0.055. This association is in the expected direction and is suggestive that we may be over estimating the signal from the enamel on the lingual side of the incisor. These and other explanations are being explored in this particular application. We are also, for other reasons as well, exploring different formulations of the EPR sensor, including making it more conformal to teeth of different sizes.

Here, we have shown the utility of ZTE MRI for EPR tooth dosimetry. Others have shown the potential applications of ZTE MRI to image samples with rapid transverse relaxation, including teeth [15,16], bone [17], and lungs [18], as well as to map tissue electrical properties [19]. At our institution, we are exploring the utility of this technique in clinical applications such as imaging maxillofacial tumors and bone remodeling in patients with complex head and neck cancers and to directly quantitate myelin in the spinal cord in patients with demyelinating disease.

5. CONCLUSIONS

High resolution ZTE MRI can be used to successfully image and quantitate tooth enamel and identify structural defects that may affect dose estimates. Our results warrant further exploration of the role of non-destructive ZTE MRI in tooth imaging for enhancing the accuracy of tooth dosimetry through surrogate representation of enamel volume. HFSS simulations of EPR estimates of dose based on the total distribution of enamel from the MRI images did not correlate well with the measured EPR signal as theory would suggest. However, HFSS based on the enamel from the front half of the tooth was in the expected direction. These results, coupled with the successful and rich imaging of enamel distribution using ZTE, warrant further study of the impact of enamel on EPR dose estimates.

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Non-selective excitation in the presence of imaging gradients

Figure 1.

The ZTE pulse sequence diagram. Non-selective sample excitation occurs in the presence of a magnetic gradient, followed rapidly by signal readout.

Figure 2.

The greyscale image is a surface representation of a full 3 dimensional B1 field distribution for a particular upper central incisor. The EPR resonator coil is shown, placed in its standard position with the top of the loop touching the enamel at 1 mm below the root and touching toward the bottom of the incisor as the tooth's contour permits. Simulated B1 results are produced using HFSS software and, when integrated across the full volume, are directly proportional to the amplitude of the RIS [14].

Figure 3.

Example of ZTE imaging showing the complete incisor with the entire tooth being immersed in water. The 3D isotropic ZTE image was acquired with 100 μm resolution in 20 minutes. ZTE MRI (a) discriminates tooth enamel effectively (the dark regions are the enamel; the upper right surface is the measured front surface of the tooth; the tip shows wear at the biting edge exposing dentin) and (b), can identify dental caries (white arrow; and other features such as wear) that may not be evident on visual inspection.

Figure 4.

Matched surface renderings of the same incisor (not one of the 10 study teeth) using both the ZTE MRI (left) and MicroCT (right); the volumes represent the segmented volumes labeled as enamel. While there is an order of magnitude differences in resolution, 100 μm vs. 11 μm , the resultant volume and geometry remains similar with volumes of 81.19 mm^3 and 81.47 mm^3 respectively.

A: Upper central incisors: Labial and side surfaces of 10 study teeth (numbered); incisal edge at the top

B: Upper central incisors: Lingual and side surfaces of study teeth (numbered); incisal edge at the top

Figure 5.
ZTE MRI-derived volumetric meshes of tooth enamel

Table 1

Measures of Enamel and Estimated Dose for the Study Teeth

Tooth	Donor	Enamel Volume [mm ^{^3}]	Height [mm]	sRIS [Gy]	mRIS [Gy]
T8-141	D1165	94.8	11.1	9.2	10.3
T9-130	D1165	108.5	10.9	10.4	8.9
T8-131	D1154	88.7	9.6	8.2	10.0
T9-118	D1154	84.4	9.4	8.9	10.8
T8-139	D1161	123.5	11.5	11.3	9.2
T9-127	D1161	102.5	11.2	10.4	9.3
T8-95	D1125	97.3	10.8	9.1	10.6
T9-83	D1125	95.5	11.4	11.1	10.2
T8-57	D1083	108.4	12.4	10.7	10.5
T9-46	D1083	109.4	12.5	10.9	10.9

Pearson Correlations (R) Among variables	Enamel Volume [mm ^{^3}]	Height [mm]	sRIS [Gy]	mRIS [Gy]
Enamel Volume [mm ^{^3}]	-	0.72 *	0.78 *	-0.39
Height [mm]	-	-	0.80 *	-0.07
sRIS [Gy]	-	-	-	-0.08

(Top): For each tooth (5 donors), measures are: summary enamel volume from the segmentation from MRI data, height at the midpoint of the labial surface using calipers, simulated RIS from HFSS (based on MRI of whole tooth), and measured RIS from EPR.

(Bottom): Pearson correlation coefficients;

* 2 sided p-value 0.05, N=10.