Human teeth/IN VIVO ESR DOSIMETRY

KHNP-RHI

2016. 5. 11

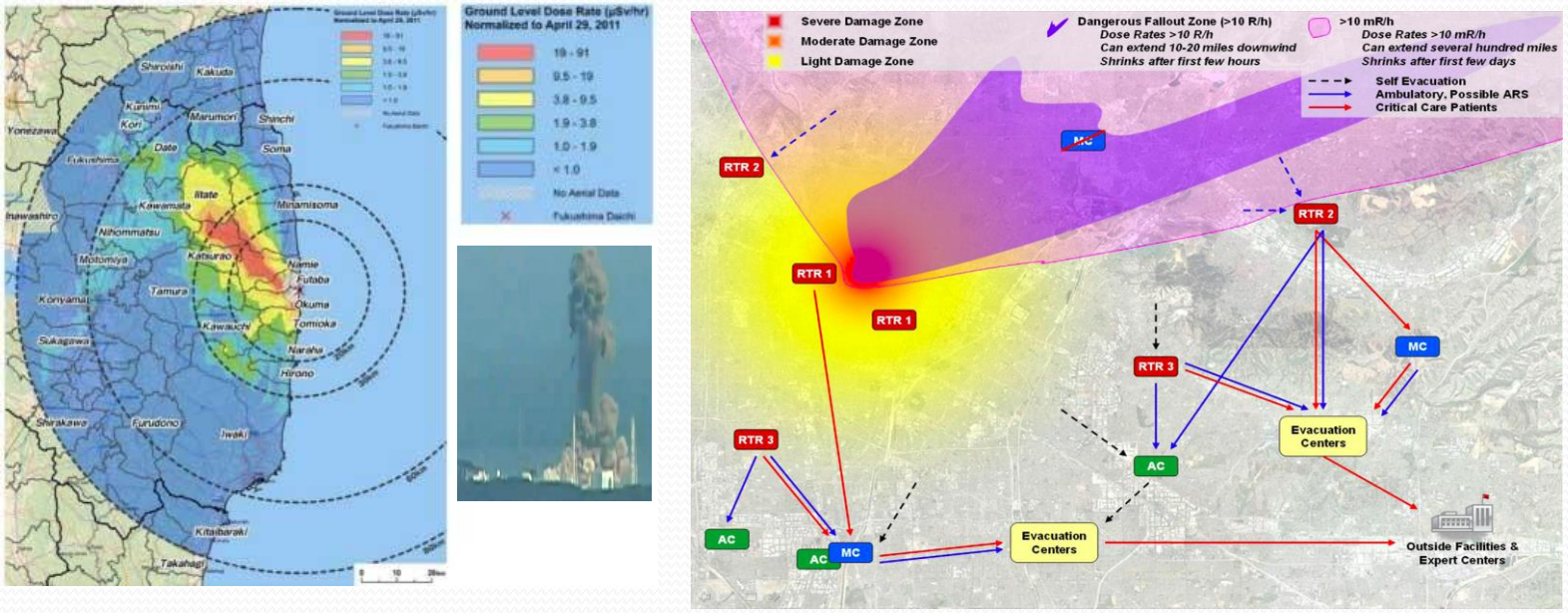
Overview

1. Radical in Enamel of Teeth induced by ionizing radiation
2. Overview of In-vivo ESR dosimeter
3. Application of In-vivo ESR dosimetry method
4. Future study

Purpose of In vivo ESR Tooth Dosimetry

1. In emergency radiation situation, triage(rapid classification) of patient into low and high exposure

2. Quantitative assessment of dose across entire plausible dose range

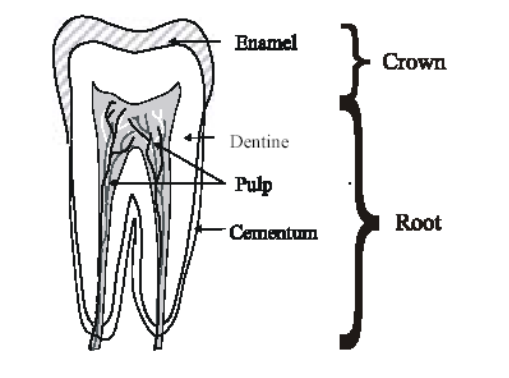


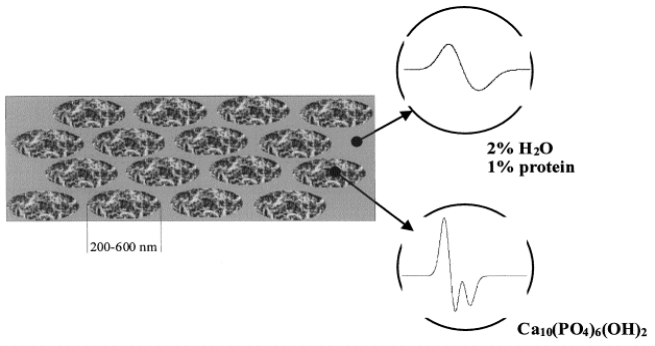
RTR=Radiation triage, treat and transport center; AC=assembly center; MC= medical center

** Respective Dosimetry Based on Long Lived Free Radicals, Harold Swartz, Geisel Medical School at Darmouth, 2015*

Radical detection by EPR spectroscopy

Radicals in human teeth



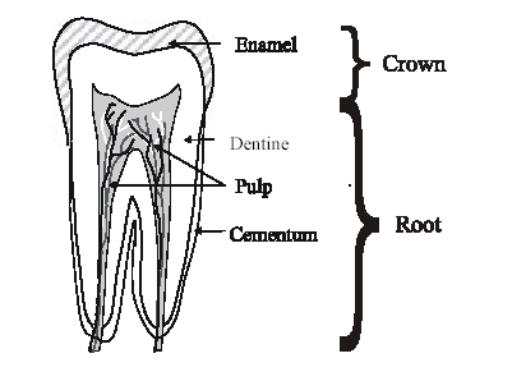


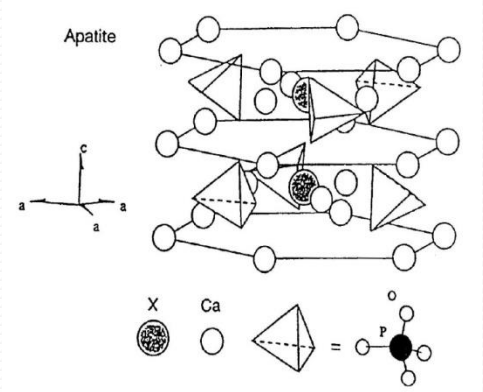
- Teeth is most stable tissue in human body(No modeling and remodeling in life time)
- Radicals in crystal structure preserved for long time(10^7 year)
- Enamel of teeth composed of 97% hydroxyapatite needle type crystalline and organic tissues
- 70 ~ 75% Dentine, 60 ~ 70% Compact bone

- ** Application of Electron Spin Resonance(Motoji Ikeya, Osaka university) 2002*

Radical detection by EPR spectroscopy

Radicals in human teeth



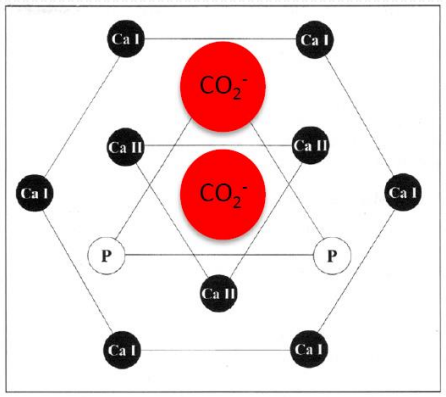


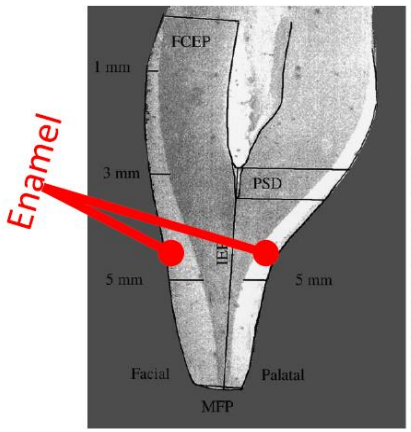
- hydroxyapatite($Ca_{10}(PO_4)_6(OH)_2$) crystal of Enamel parts is hexagonal microcrystalline structure
- Measuring of Carbon dioxide radical anion (Co_2^-) caused by high energy photons or neutrons in hydroxyapatite($Ca_{10}(PO_4)_6(OH)_2$) crystal of enamel parts

** Application of Electron Spin Resonance(Motoji Ikeya, Osaka university) 2002*

Radical detection by EPR spectroscopy

Radicals in human teeth

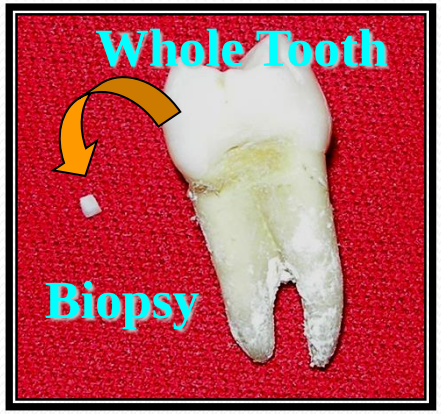


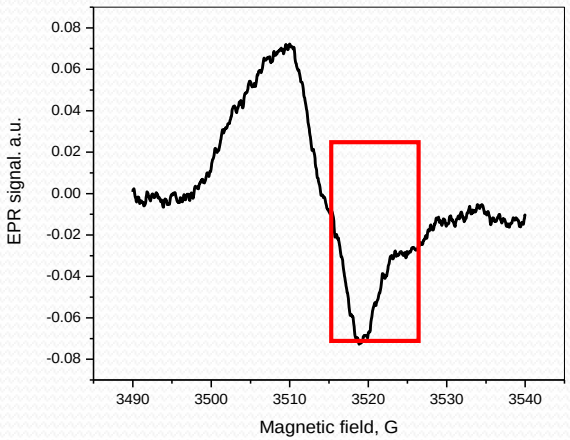


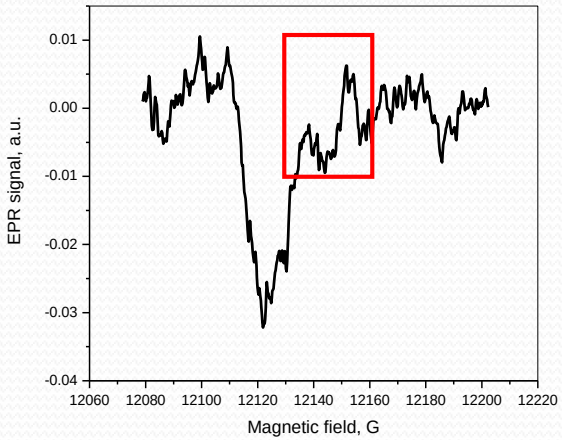
- Ionizing Radiation induces the creation of radicals in the native calcium hydroxyapatite matrix
- Radical concentration is proportional to dose quantity(transferred energy)
- In vivo ESR detect the presence of radicals
- Radical Production in Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$
  - * Carbonate at environmental tissue replace hydroxyl or phosphate
  - * ionizing radiation converts carbonate impurities into CO_2^- radicals

** Background and instrumental methods for ESR Tooth dosimetry Wilson Shreiber clin-ESR, LLC 2014*

Radical detection by EPR spectroscopy







- Small amount of enamel biopsy technique a small enamel chip is removed from tooth crown
- Teeth restoration using light-cured composite resins rapidly restore small enamel defect
- Center : X-band(100 mg), 0.1 Gy, Right : Q-band(4 mg), 0.1 Gy
- Q-band has significantly less amount of the sample required for dose measurement and has significantly better spectral resolution of dose response

** Electron Paramagnetic Resonance Biodosimetry in Teeth and Fingernails, A. Romanyukha, Naval Dosimetry Center,8901 Wisconsin Ave., Bethesda, MD, 20889,USA*

Low frequency EPR

- Biological samples are **aqueous** and undergo 'non-resonant' **absorption** of microwave energy and hence poor **penetration depth.**
  The frequency of the instrumentation is reduced to overcome this problem

	~300 MHz	~750 MHz	1-2 GHz	~3 GHz	9-10 GHz
Penetration Depth	> 10 cm	6-8 cm	1-1.5 cm	1-3 mm	1 mm
Objects studied	Mouse, rat	Frequency	Mouse, rat heart, **Teeth**	Mouse tail Topical (skin)	In vitro samples (~100 uL vol.)

Basic structure of In vitro ESR

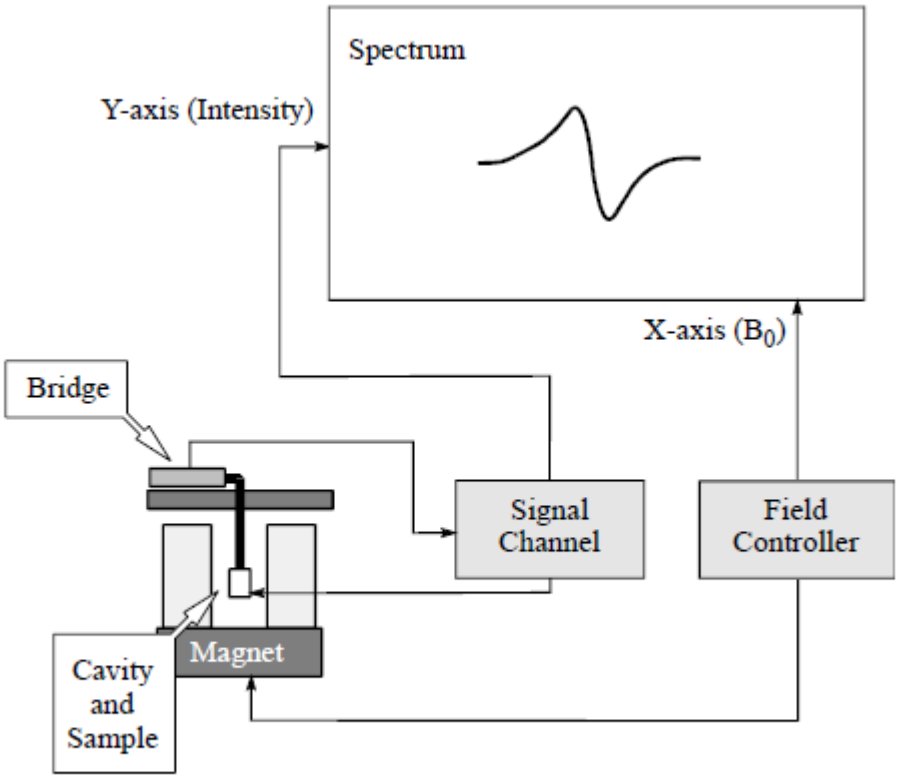


Figure 2-19 Block diagram of an EPR spectrometer.

PERGAMON Applied Radiation and Isotopes 52 (2000) 1031–1038
www.elsevier.com/locate/apradiso

In vivo EPR dosimetry of accidental exposures to radiation: experimental results indicating the feasibility of practical use in human subjects

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Abstract

Low frequency electron paramagnetic resonance (EPR) provides the potential advantage of making accurate and sensitive measurements of absorbed radiation dose in teeth in situ, i.e. without removing the teeth from the potential victim. The potential limiting factors for making such measurements are: (1) whether low frequency EPR is sufficiently sensitive to detect radiation-induced signal in human teeth; (2) whether sufficient sensitivity can be maintained under in vivo conditions. In this manuscript, we summarize results indicating that this approach is feasible. Using 1.2 GHz EPR spectroscopy, we found that the lower limit for these measurements in isolated human teeth is 0.2 Gy or lower. Measurements of radiation-induced EPR signals in the teeth of living rats were achieved with sufficient sensitivity to indicate that, when taking into consideration the larger mass of human teeth, similar measurements in human teeth in situ would provide sensitivity in the dose range for potential accidental exposures. We estimate that the current lower limit for detecting radiation doses in human teeth in situ (in vivo) is 0.5–1.0 Gy; this would be sufficient for determining if a person has been exposed to potentially life threatening doses of ionizing radiation. The limiting factor for sensitivity appears to be background signals rather than signal/noise, and there are feasible means to overcome this problem and further increase sensitivity. The additional instrumental developments required to make an effective in vivo EPR dosimetric spectrometer for the measurements in teeth in human subjects in situ, seem quite achievable.

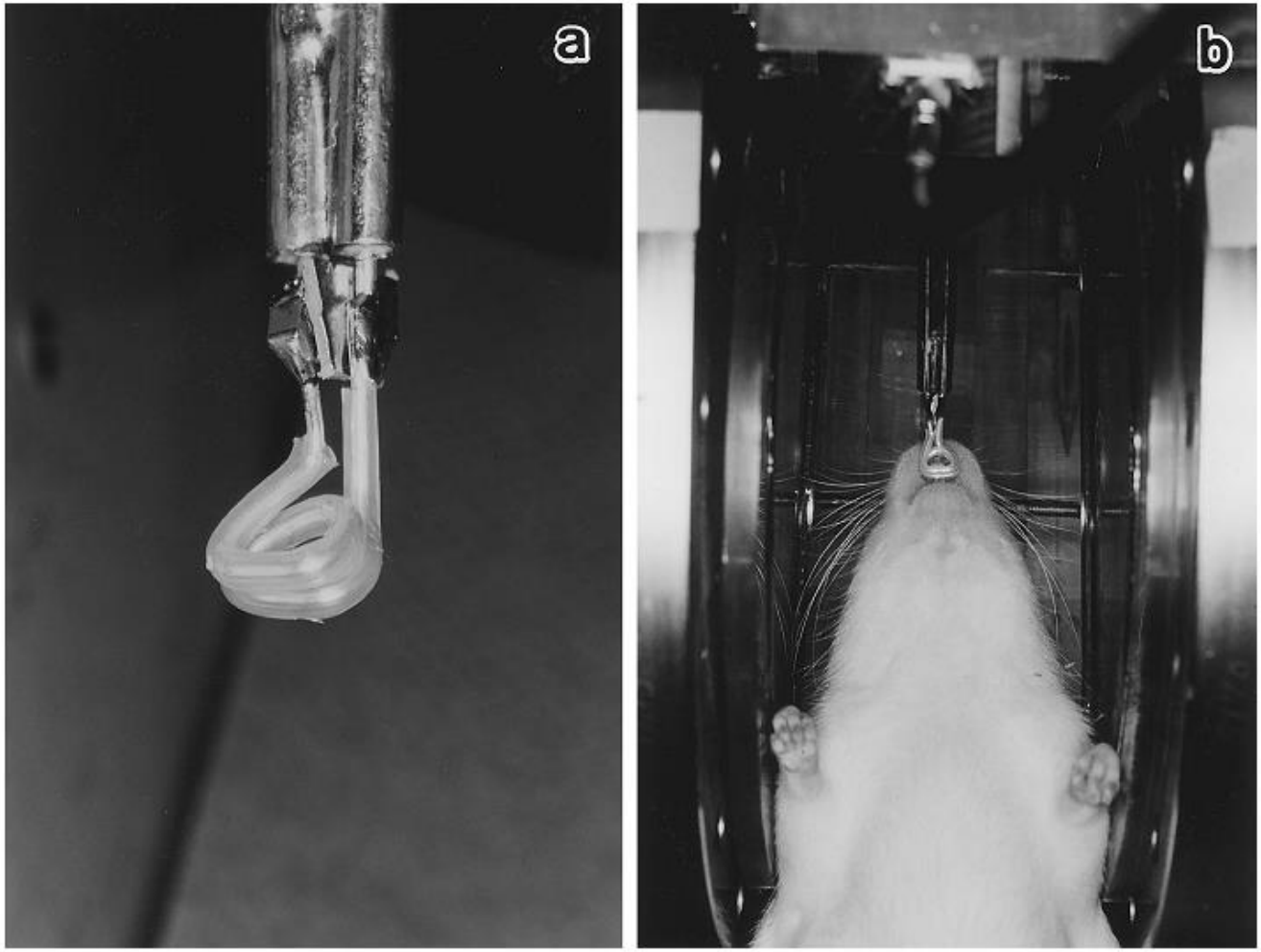

Fig. 3. The specially designed resonator for use in the mouth of living rats. (a) Illustration of the twin spiral loop gap resonator which has 5.0 mm internal diameter; it is a varactor tuned surface coil. (b) Illustration of the measurement in live rats; the EPR signal is detected from the upper pair of incisors, under anesthesia.

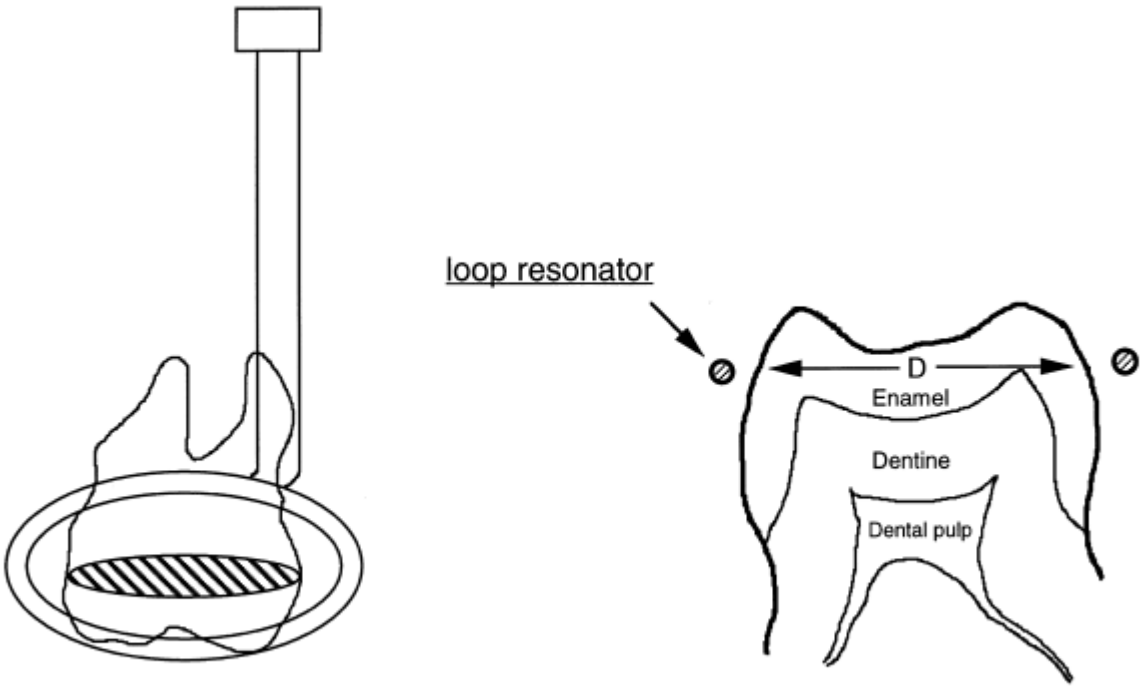

Fig. 2. Schema of the measurements in human teeth. The intensity was normalized to the unit area of enamel surrounded by the loop resonator.

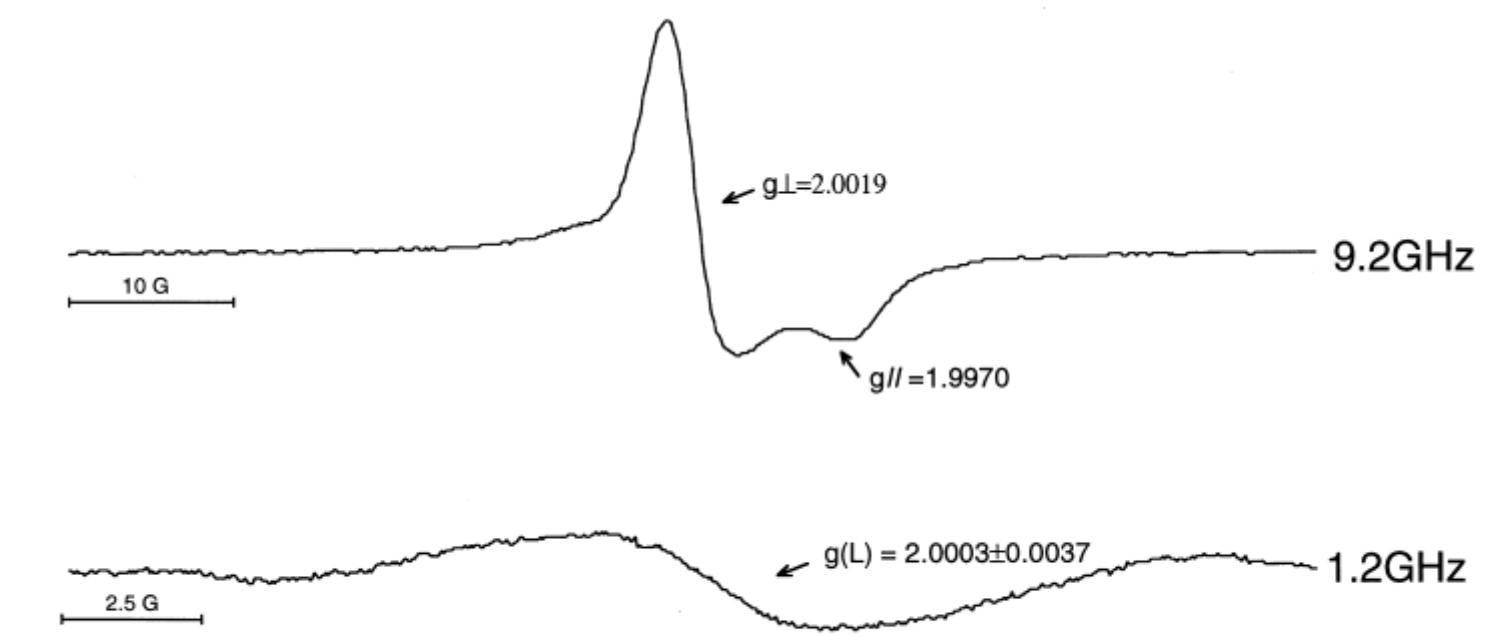

Fig. 4. Radiation-induced signal of the same sample measured by EPR at two frequencies. The sample was a pair of isolated rat teeth, 90.3 mg dry weight and irradiated with 40 Gy.

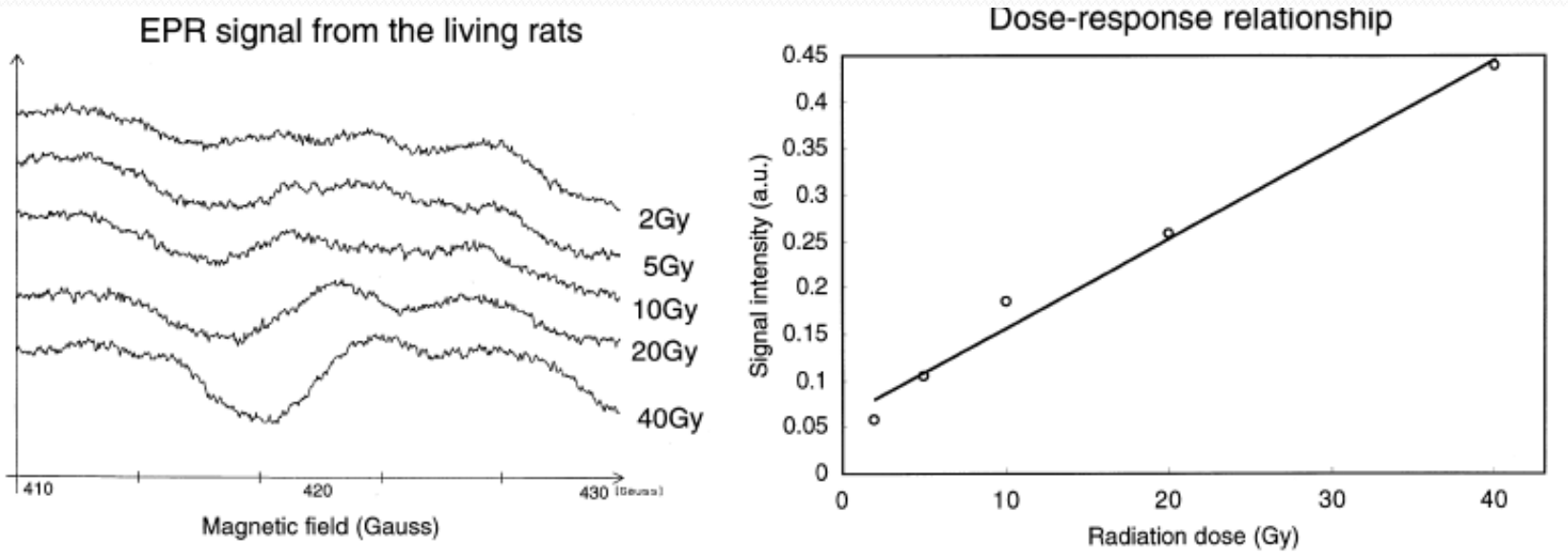

Fig. 9. In vivo EPR spectra in living rats using the specially designed resonator. Each point is based on the average from two rats. Parameters include: scan range 20 G, time constant 0.1 s, scan time 40 s, modulation amp. 1.6 G, 30 sweeps.

Overview of In vivo ESR Dosimeter Resonator Placement

L-band(~1GHz) spectroscopy effective than X-band

- work with whole teeth in vivo
- less absorbed by water
- sensitivity loss overcome by volume

(10mm vs 1mm : L-band :X-band)

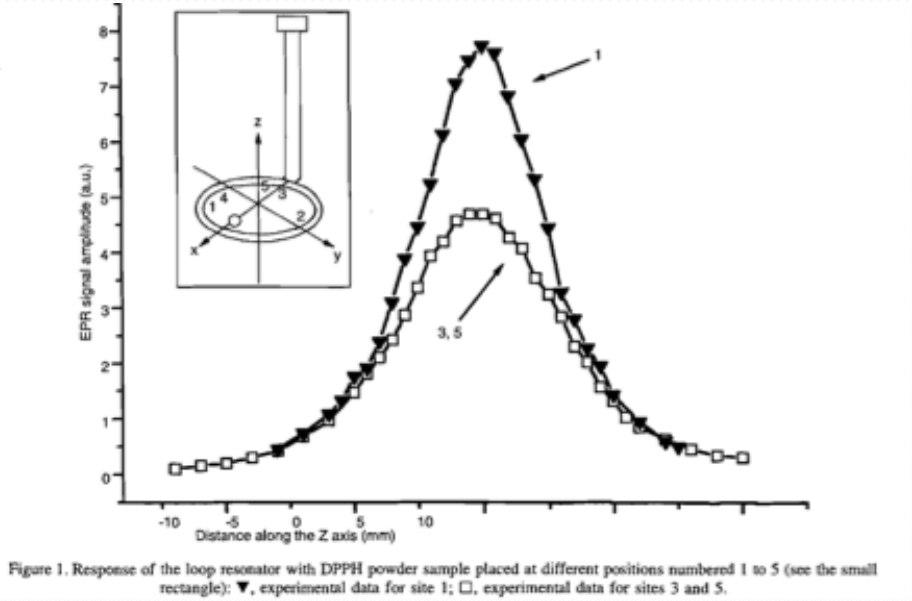

Figure 1. Response of the loop resonator with DPPH powder sample placed at different positions numbered 1 to 5 (see the small rectangle): ▼, experimental data for site 1; □, experimental data for sites 3 and 5.

1. SITE No 1(opposite to the wave guide) : Most Sensitive
2. Distance along z-axies : z= 5mm :strong z=0 mm: weak
3. 1mm outside athena : 7% of SITE No1
4. Z=+5 mm or -5 mm almost same, outside decrease (0.20,0.26,0.30,0.25,0.33) signal shape not change. g=2.0036

Overview of In vivo ESR Dosimeter Resonator Placement

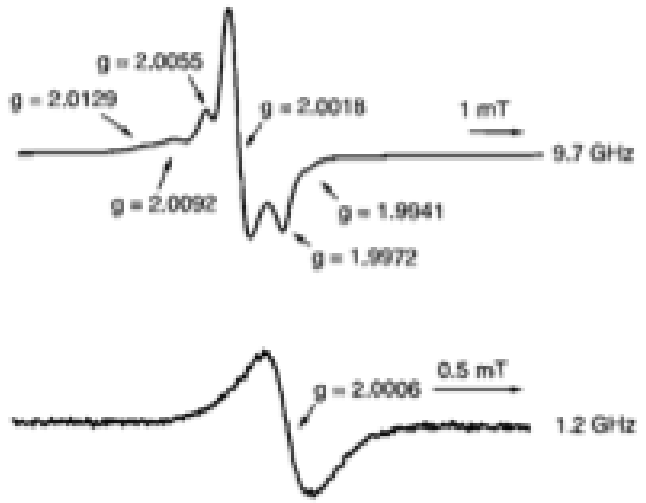

Figure 3. X-band and L-band (loop resonator) EPR spectra of a 875 Gy-irradiated whole human tooth.

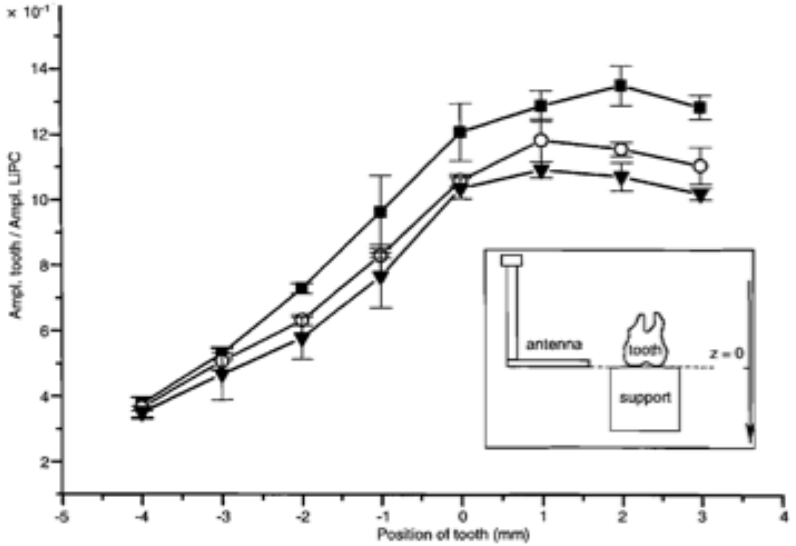

Figure 5. Relative EPR signal amplitudes (see text) obtained with the loop resonator for different components of one irradiated molar: ■, whole tooth with root; ○, full crown (enamel and dentin); ▼, empty crown (only enamel).

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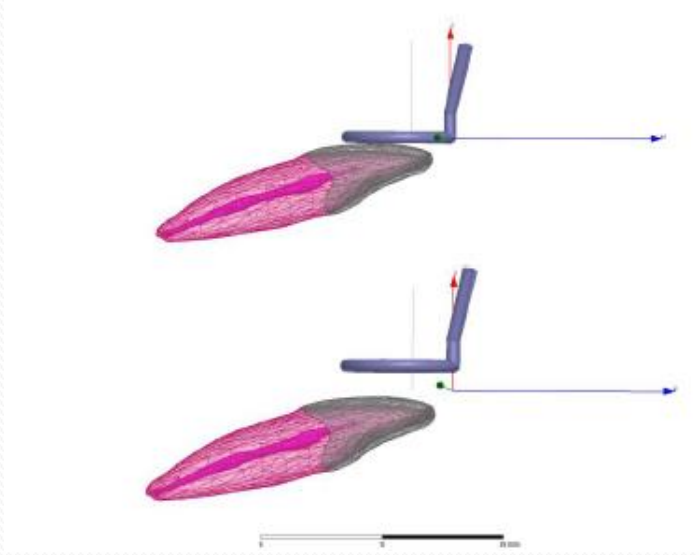

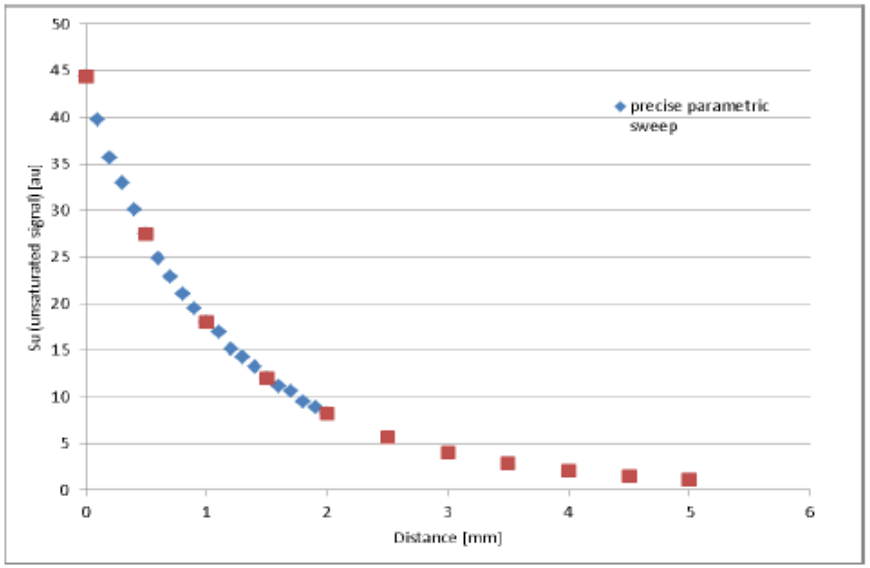

** Background and instrumental methods for ESR Tooth dosimetry Wilson Shreiber clin-ESR, LLC 2014*

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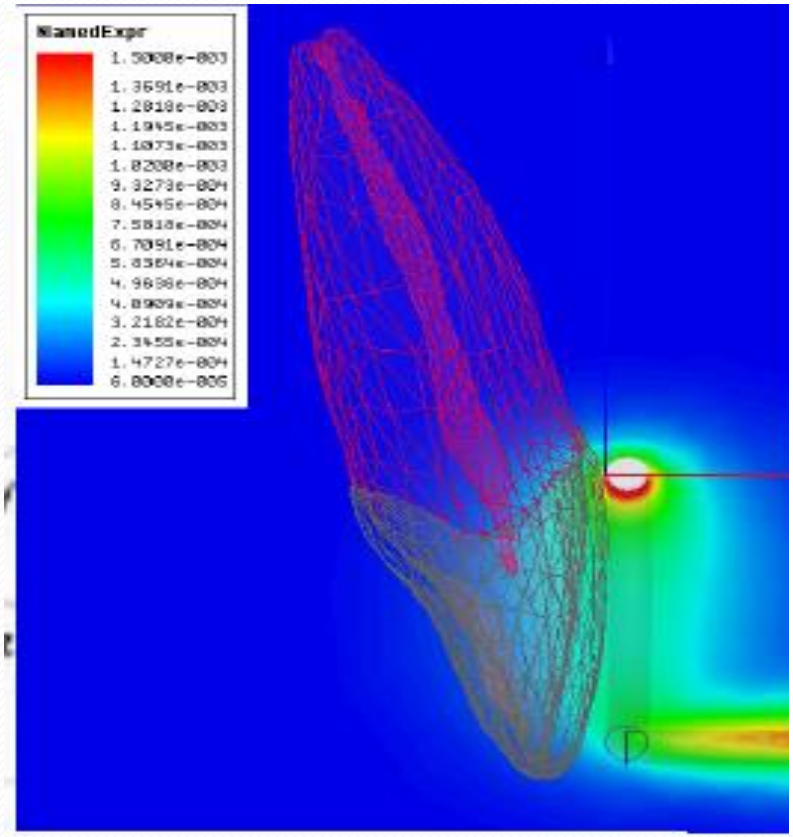

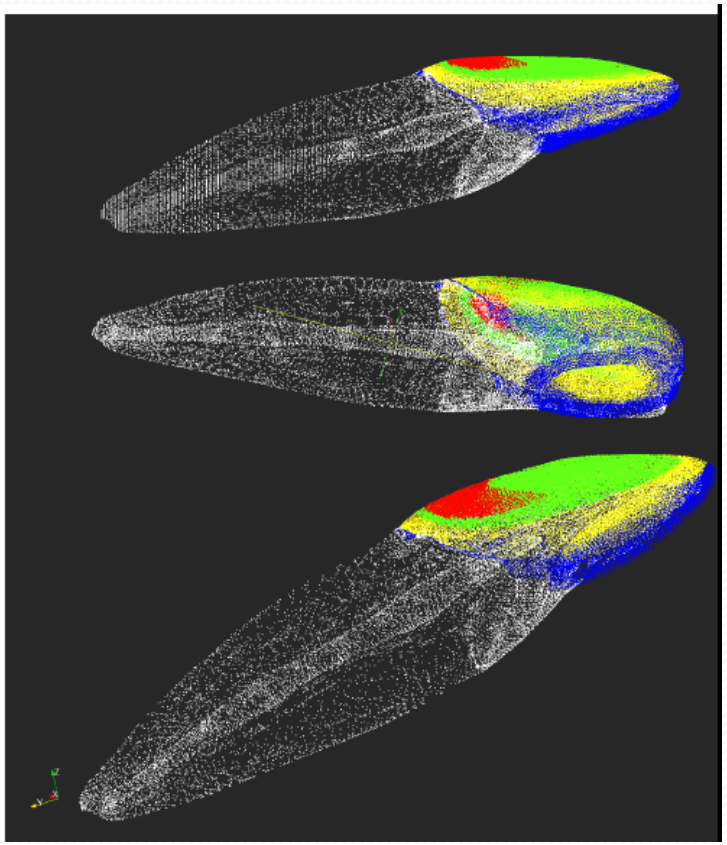

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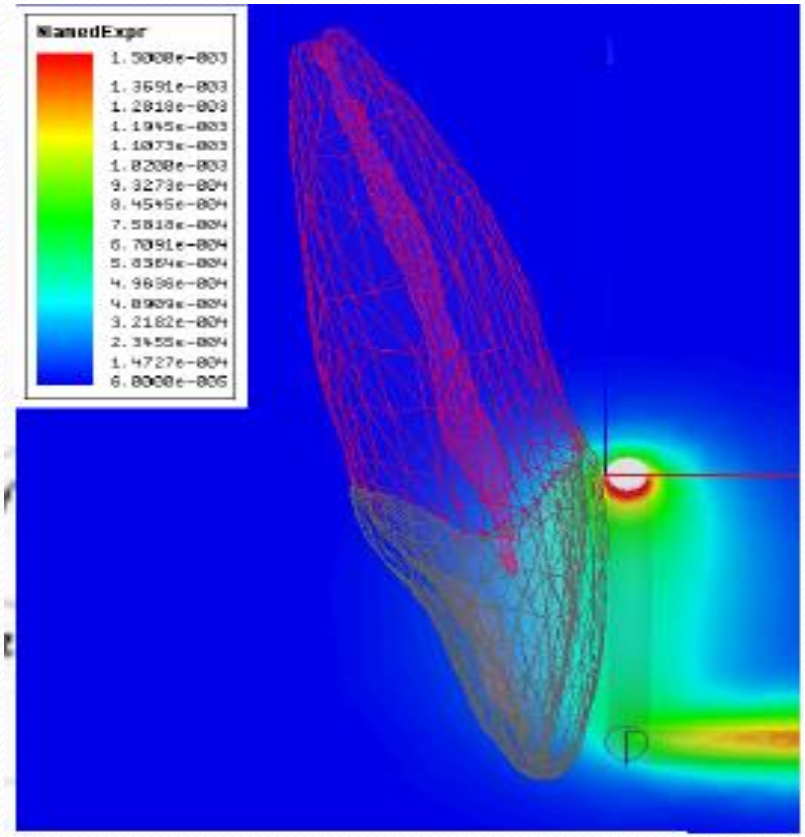

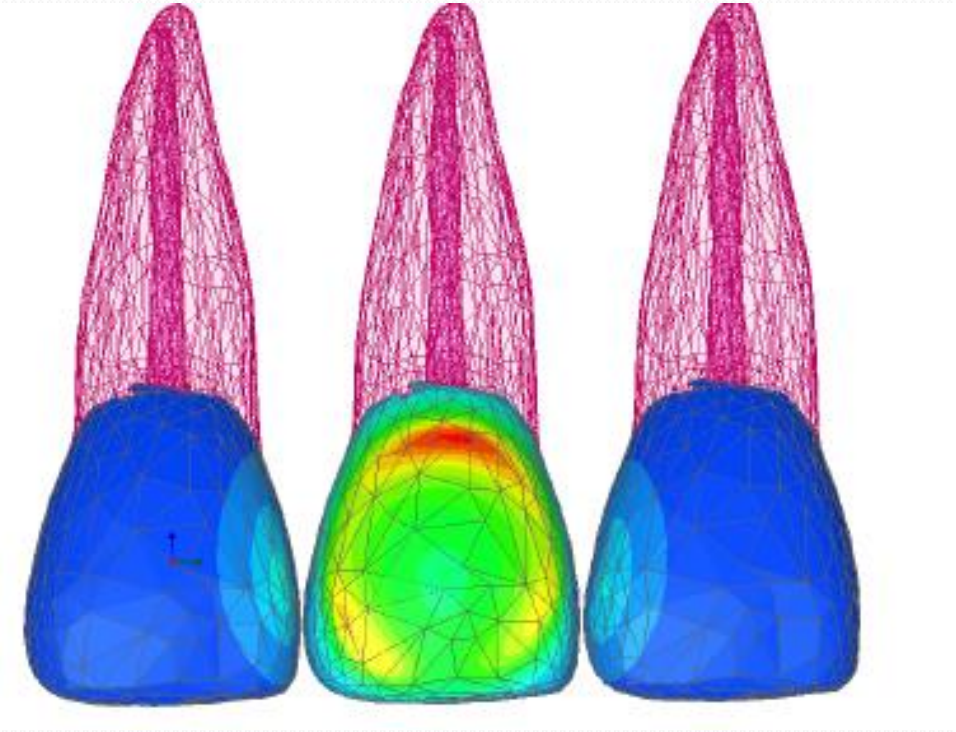

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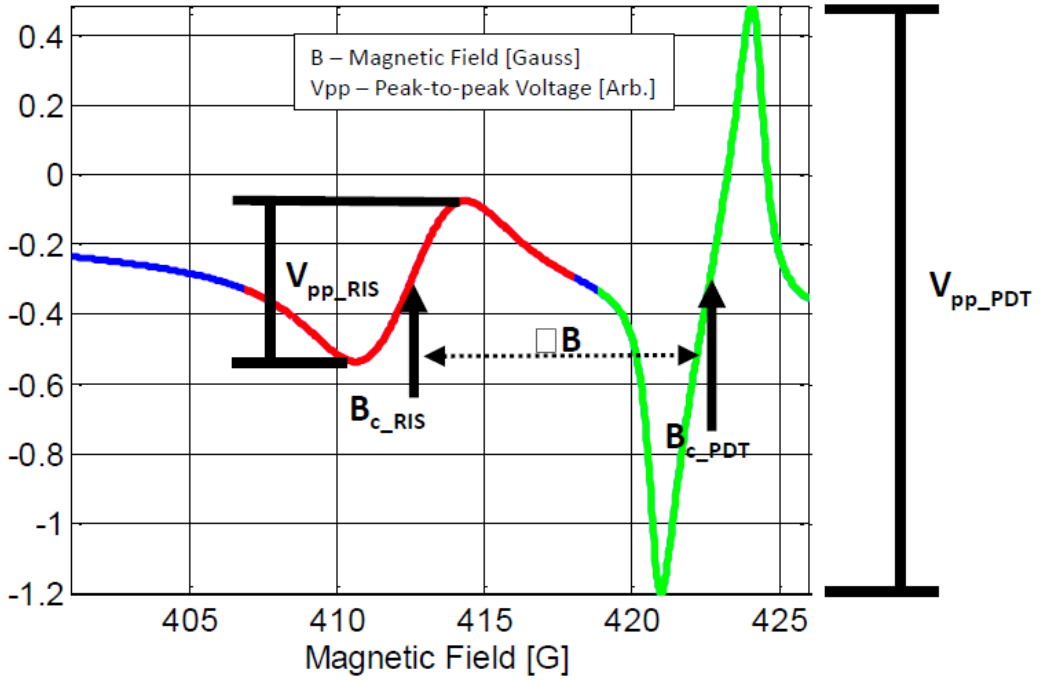
Overview of In vivo ESR Dosimeter
EPR Spectra of Teeth

Radiation Induced Signal (RIS)



EPR Reference Standard (N-15 PDT)

* N15-PDT : N^{15} – labeled and Perdeuterated Tempone

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Overview of In vivo ESR Dosimeter

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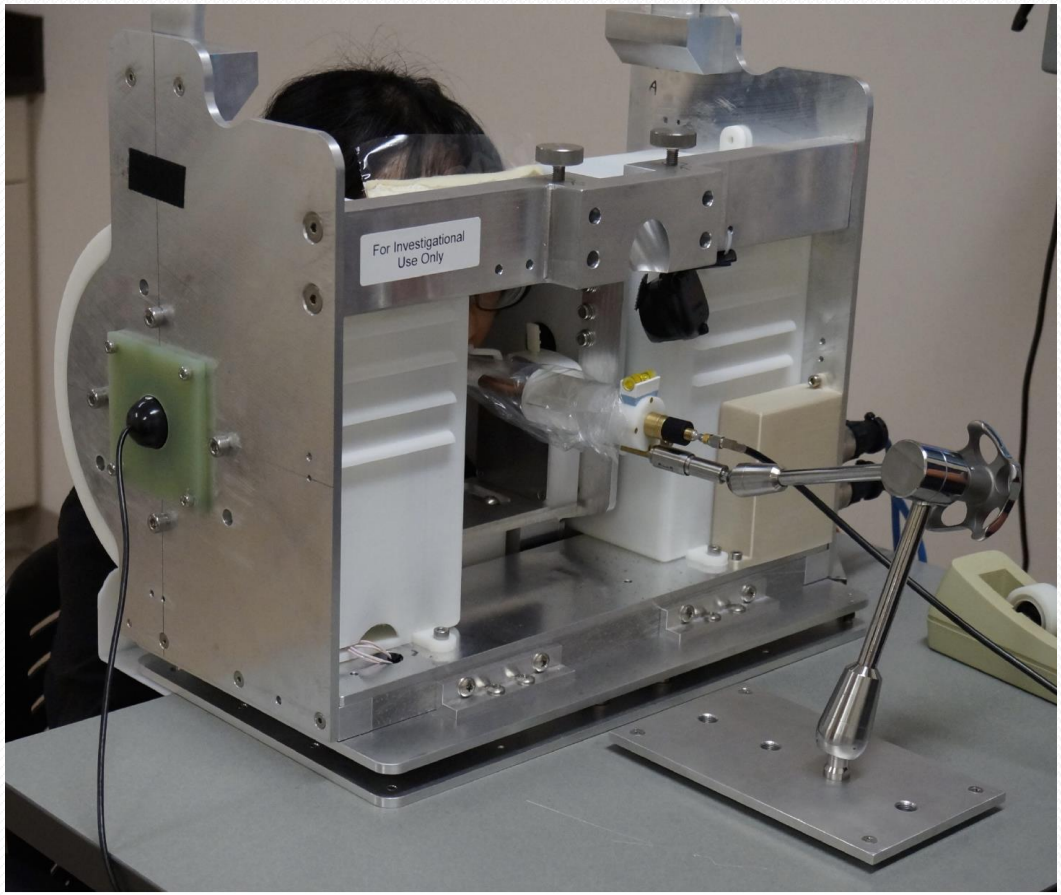
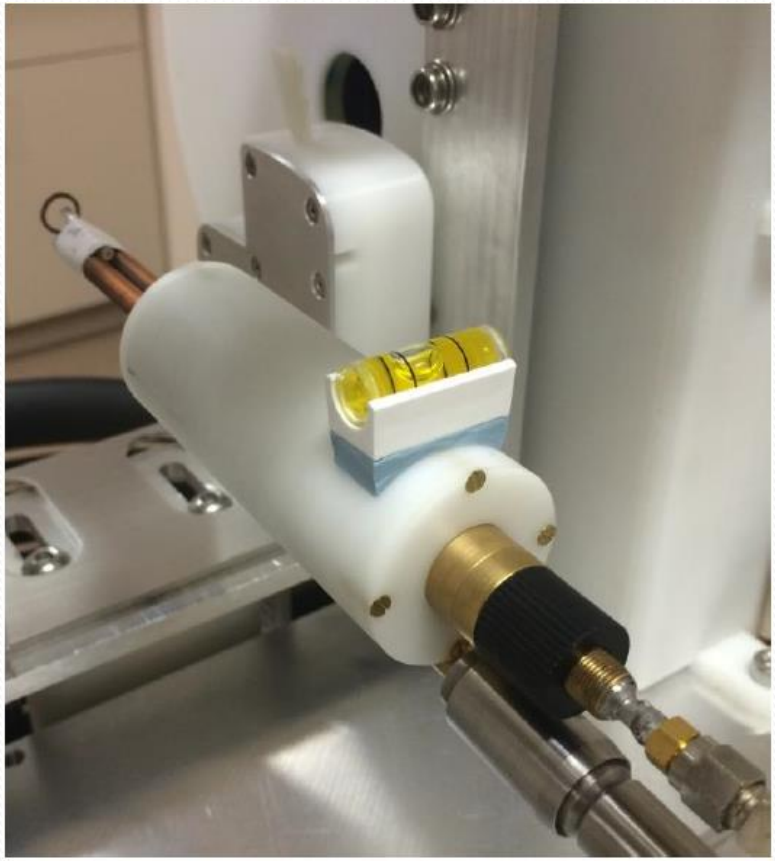
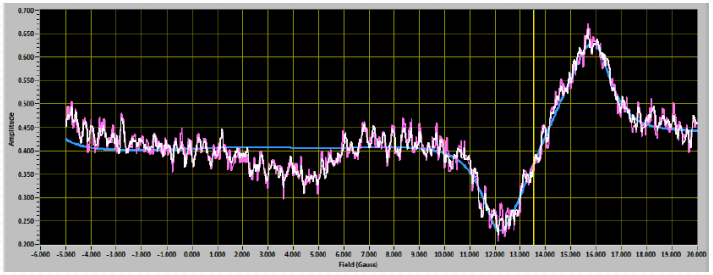
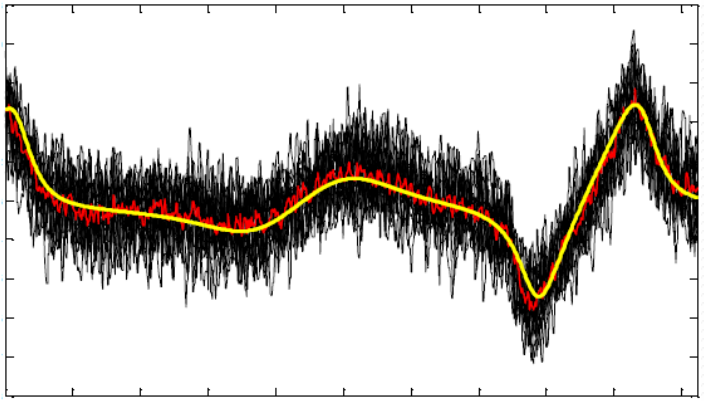


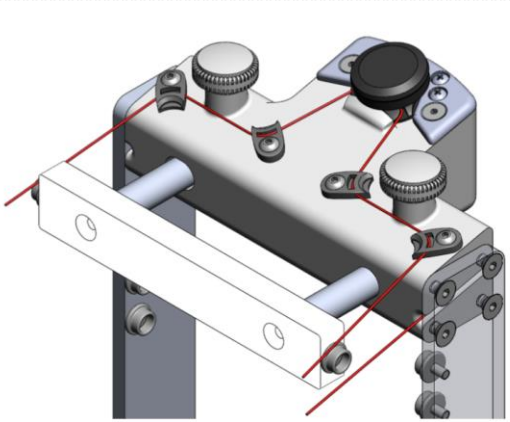
Overview of In vivo ESR Dosimeter
Resonator Placement

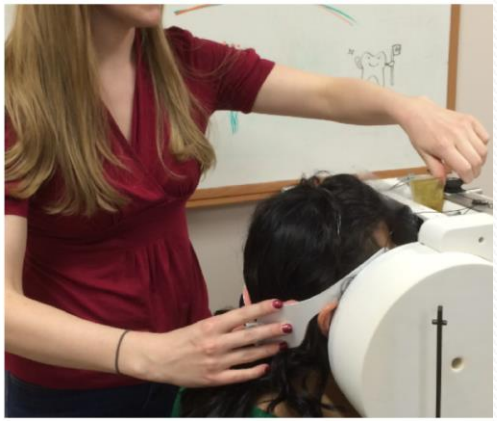






Overview of In vivo ESR Dosimeter
Patient Positioning





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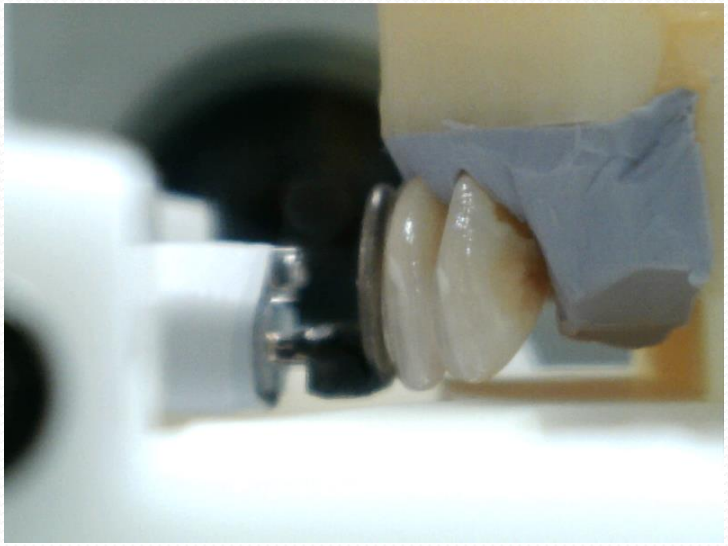
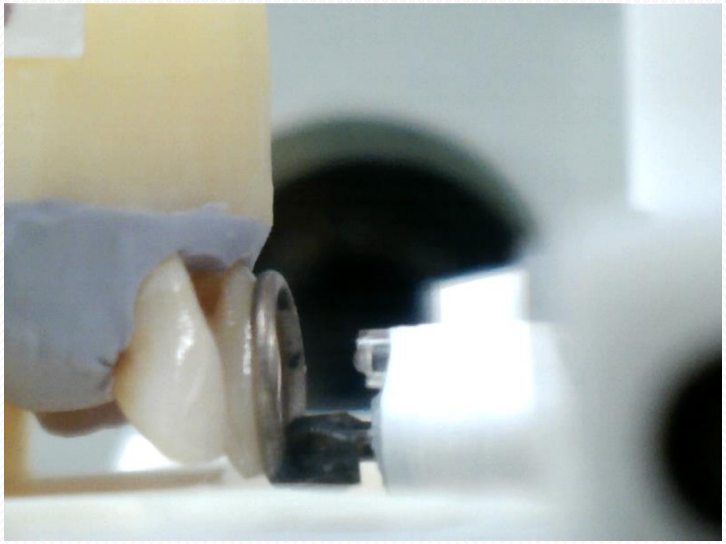
Application of In vivo ESR dosimetry - Example of ESR Spectrum





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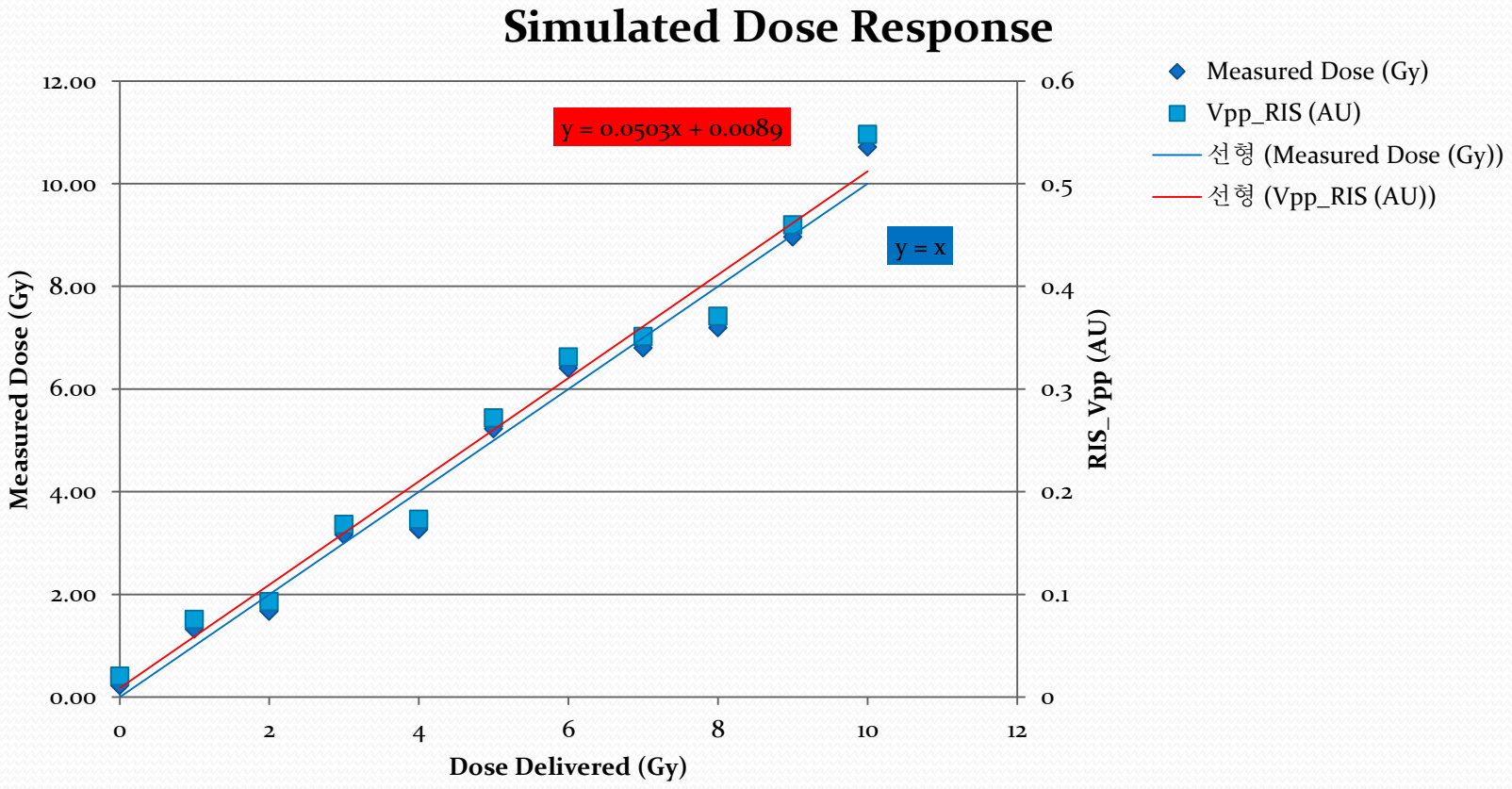

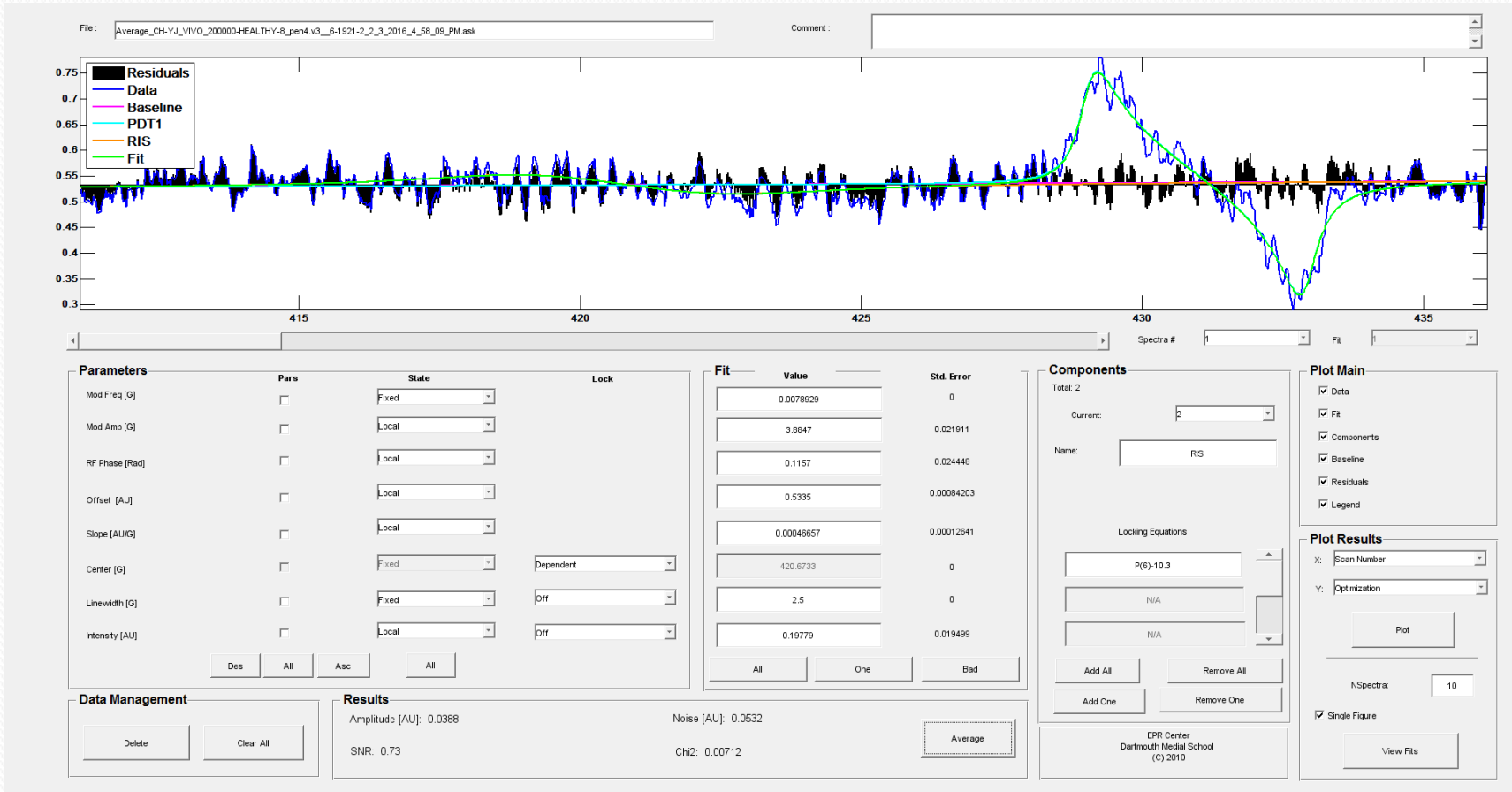
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Remove One
EPR Center
Dartmouth Medial School
(C) 2010
Plot Main
Data
Fit
Components
Baseline
Residuals
Legend
Plot Results
X:
Scan Number
Y:
Optimization
Plot
NSpectra:
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Single Figure
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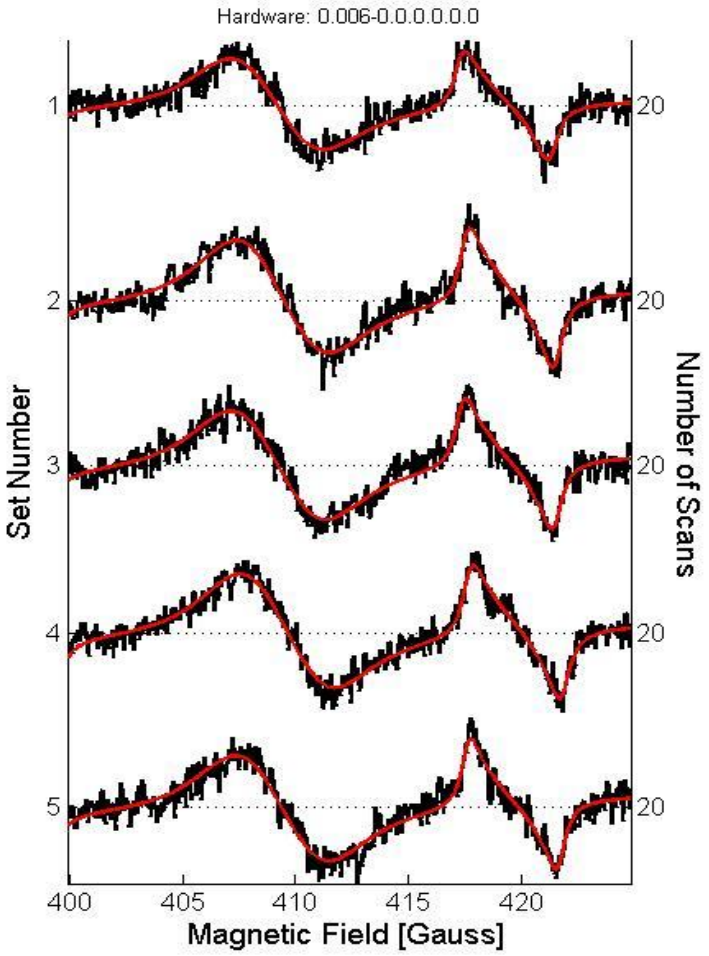
Chi2: 0.00712
Average



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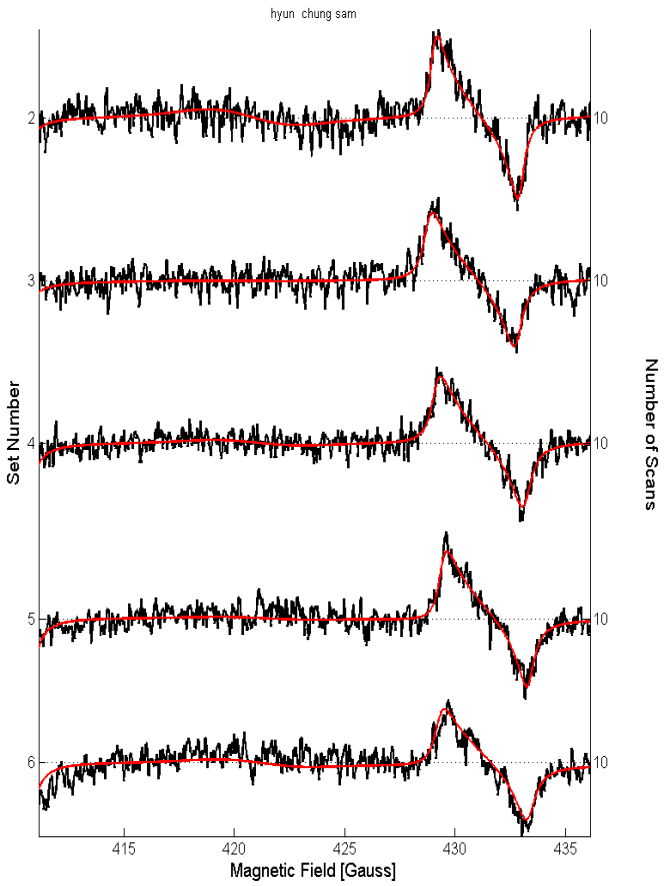

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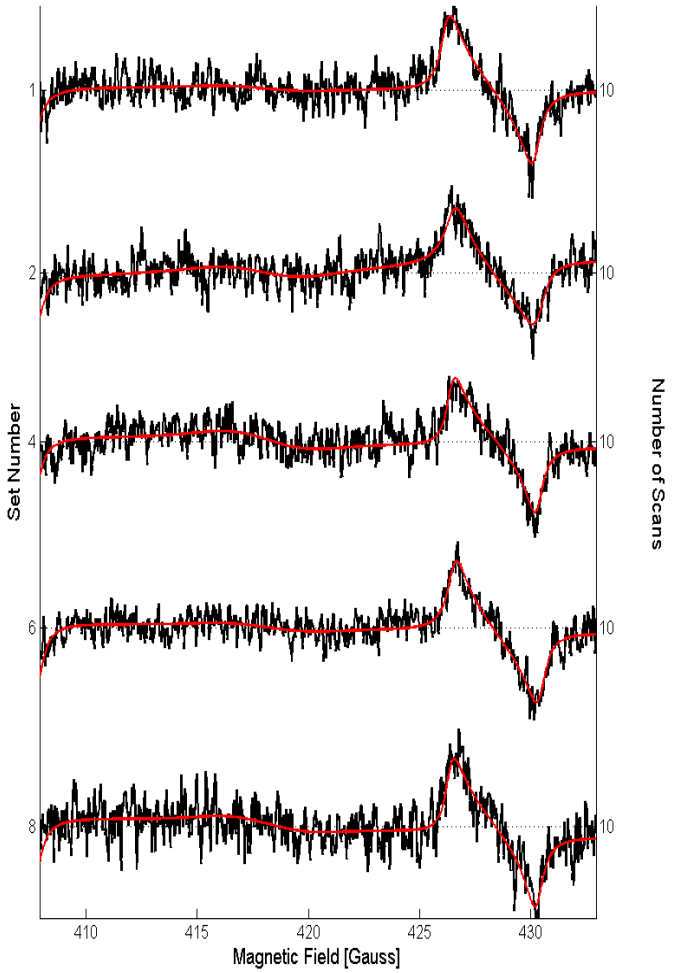
Model Name: OneCompRISTwoPDT, Online C Fit

Report Generated: 03/30/2016

Collection: 02/03/2016, 4:58 PM - 5:02 PM, Elapsed: 00:04:28

Data Parameters	Value
Reference phase [deg]	-3
Scan range [G]	25
Sensitivity [uV]	0.5
Scan time [s]	3
Modulation amplitude [G]	4
Gradient [A]	0
Central field [G]	423.623
Attenuation [dB]	5
Time constant [ms]	5
Modulation frequency [Hz]	22100
RF frequency [GHz]	**1.1546 - 1.156**
Sweep Calibration [G/Vrms]	4.75
Modulation Calibration [G/Vrms]	4.85
Q-start	41
Q-end	0
Freq Voltage	**-1.41 - -0.77**
Phase Voltage	0.53
In Phase Offset	**0.51 - 0.58**
Out Phase Offset	**-1.33 - -0.85**

Set:	PDT Vpp:	RIS Vpp:	PDT: SNR:	RIS SNR:
2	0.448	0.0443	7.28	0.72
3	0.368	0.00271	6.76	**0.0498**
4	0.358	0.0161	8.02	0.36
5	0.371	0.00696	7.56	0.142
6	**0.304**	0.0198	**5.24**	0.341
Mean:	0.37	0.018	6.97	0.323
SD:	0.0514	0.0162	1.07	0.258
SD/Mean:	0.1391	0.90363	0.15357	0.80101



File Prefix: CH-YJ_VIVO_200000-HEALTHY-9_pen4.v3__6-1930

Model Name: OneCompRISTwoPDT, Online C Fit

Report Generated: 03/30/2016

Collection: 02/12/2016, 1:54 PM - 2:11 PM, Elapsed: 00:17:16

Data Parameters	Value
Reference phase [deg]	-3
Scan range [G]	25
Sensitivity [uV]	0.5
Scan time [s]	3
Modulation amplitude [G]	4
Gradient [A]	0
Central field [G]	420.415 - 420.426
Attenuation [dB]	5
Time constant [ms]	5
Modulation frequency [Hz]	22100
RF frequency [GHz]	1.1537 - 1.1549
Sweep Calibration [G/Vrms]	4.75
Modulation Calibration [G/Vrms]	4.85
Q-start	41
Q-end	0
Freq Voltage	-0.96 - -0.43
Phase Voltage	0.28
In Phase Offset	0.42 - 0.48
Out Phase Offset	-1.14 - -0.82

Set:	PDT Vpp:	RIS Vpp:	PDT: SNR:	RIS SNR:
1	0.472	0.0148	5.64	0.177
2	0.38	0.0406	4.43	0.473
4	0.428	0.0528	4.88	0.602
6	0.449	0.0226	6.18	0.311
8	0.467	0.0406	4.31	0.375
Mean:	0.439	0.0343	5.09	0.388
SD:	0.0373	0.0153	0.803	0.161
SD/Mean:	0.084962	0.44625	0.15784	0.41495