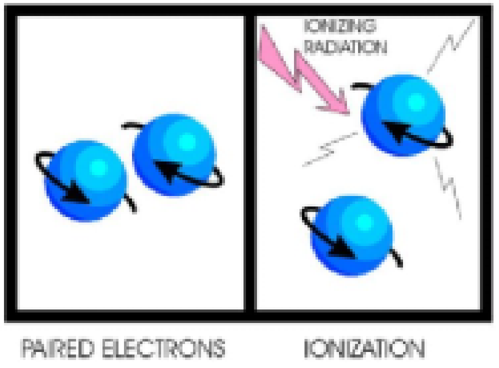
Radiation Biodosimetry I: EPR/Teeth



David A. Schauer, ScD, CHP

Executive Director

National Council on Radiation Protection and Measurements

Outline

- Radiation Biodosimetry
- Electron Paramagnetic Resonance (EPR)
  - Fundamentals, Principles and Hardware
- EPR Biodosimetry – Teeth
  - Fundamentals
  - Dose Reconstruction Protocol
  - Intercomparisons and Applications
  - Issues/Future Development
- EPR Biodosimetry – Bone
  - Fundamentals and Applications
- Conclusions

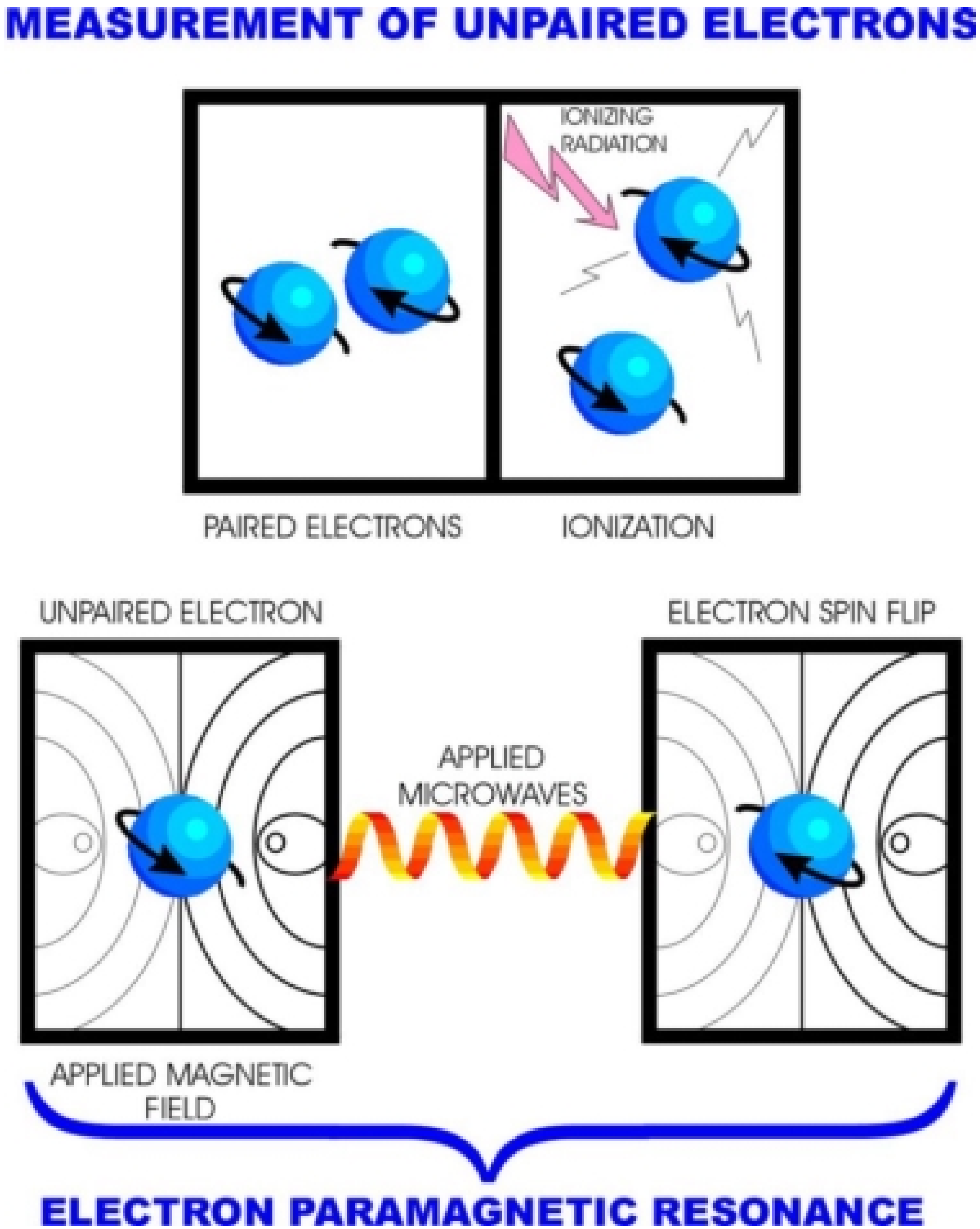
Radiation Biodosimetry

- Dose estimation based on measurement of radiation-induced changes in the body.
- Biological dosimeter requirements:
  - Measured in easily obtained fluids or tissues (?).
  - Effect should be specific for ionizing radiation.
  - Response changes as a function of dose.
  - Evaluation should be either easy and rapid, or capable of automation.

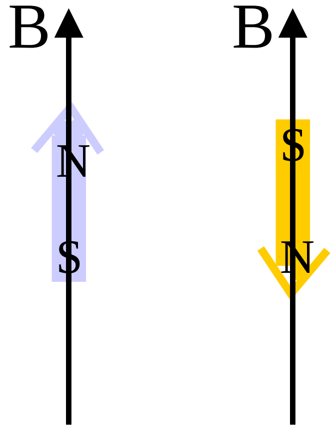
Electron Paramagnetic Resonance

- What is EPR?
  - Non-destructive magnetic resonance technique used to detect and quantify unpaired electrons.
  - Absorption of ionizing radiation generates unpaired electrons (*i.e.*, paramagnetic centers).
  - The concentration of radiation-induced paramagnetic centers is proportional to the absorbed dose.

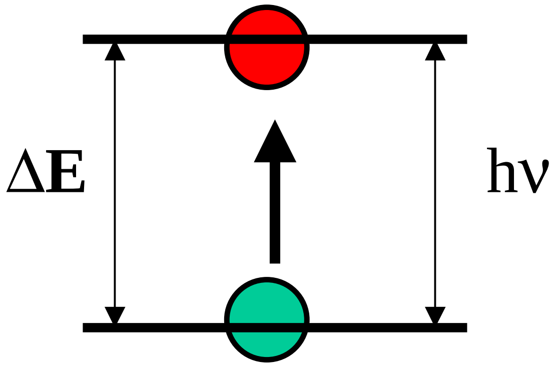
EPR Fundamentals



EPR Fundamentals
(Principles)



Electrons in magnetic field have 2 states with 2 different energies.

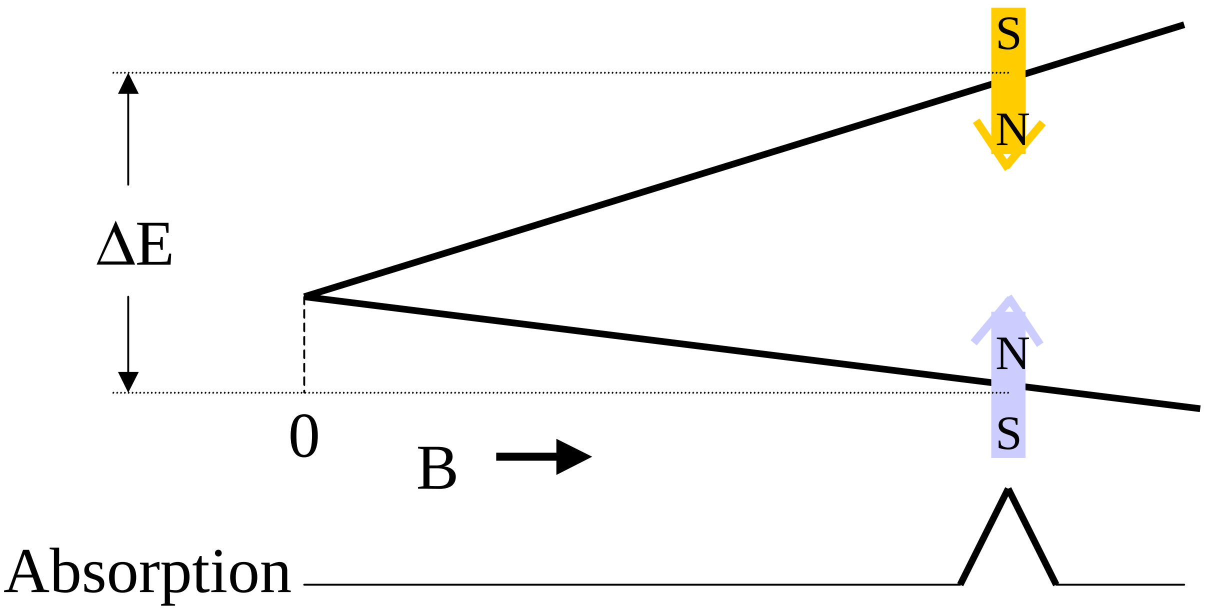


Transition between 2 levels is possible under resonance condition:

$$h\nu = g\mu_B \mathbf{B}$$

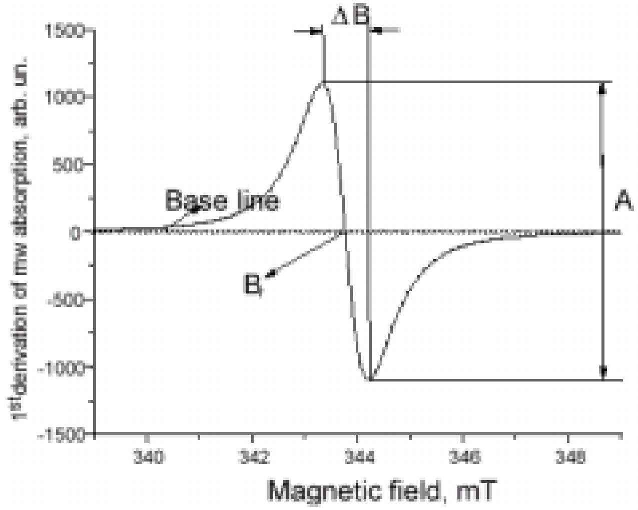
EPR Fundamentals
(Principles)

Variation of the spin state energies as a function of the applied magnetic field:

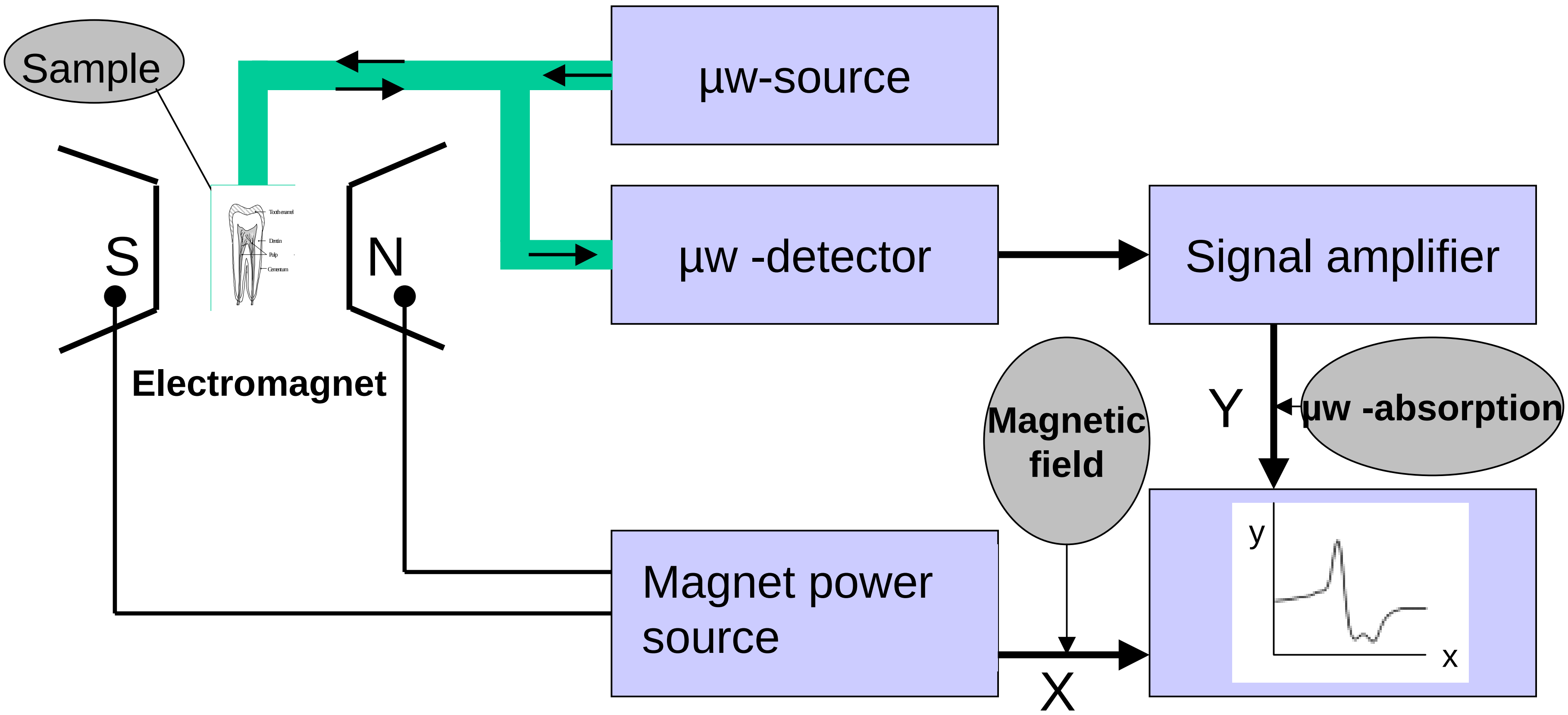


EPR Fundamentals (Hardware)

- Electromagnet
  - Regulated power supply to provide scanning of the resonance conditions.
- Microwave Module
  - Microwave generator, microwave cavity and detector(s).
- Signal Channel
  - Amplify and record microwave absorption by the sample during the magnetic field scan through the resonance condition.



EPR Spectrometer



EPR Fundamentals
(Hardware)

- L-band (1-2 GHz)
- X-band (8-10 GHz)
- Q-band (35 GHz)

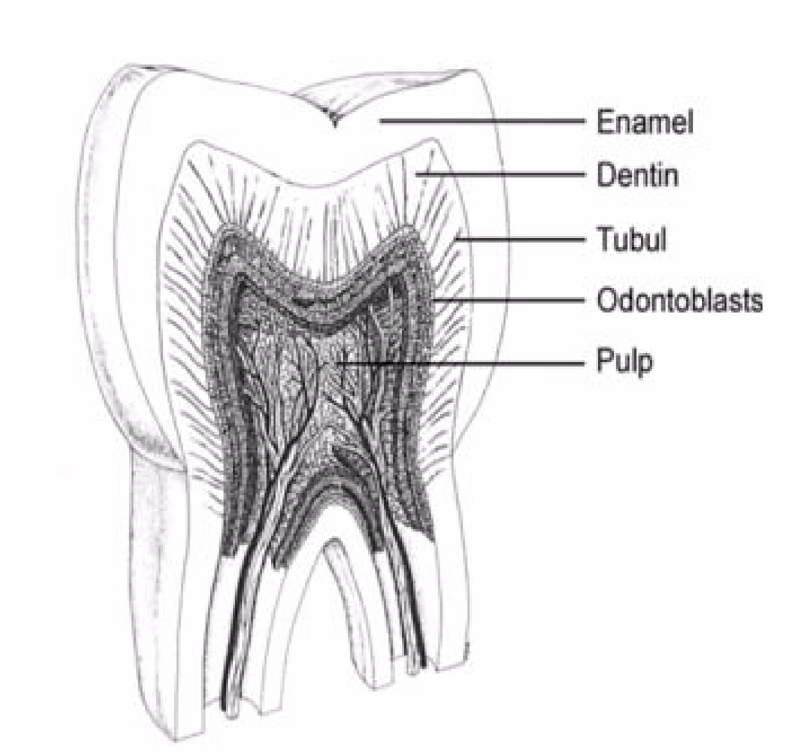
Frequency determines sample size according to:

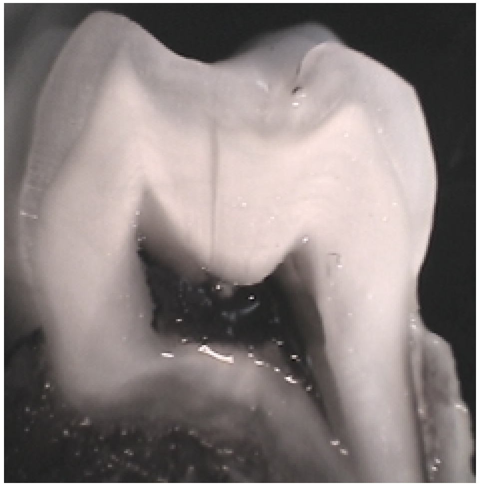
$$c = f \cdot \lambda$$

EPR Fundamentals (Hardware)

- L-band
  - For large biological samples, including organs and small animals.
- X-band
  - The most common microwave frequency.
    - Combines high sensitivity with convenient sample sizes.
- Q-band
  - For high sensitivity measurement of small samples as well as multi-frequency studies.

EPR Biodosimetry – Teeth (Fundamentals)

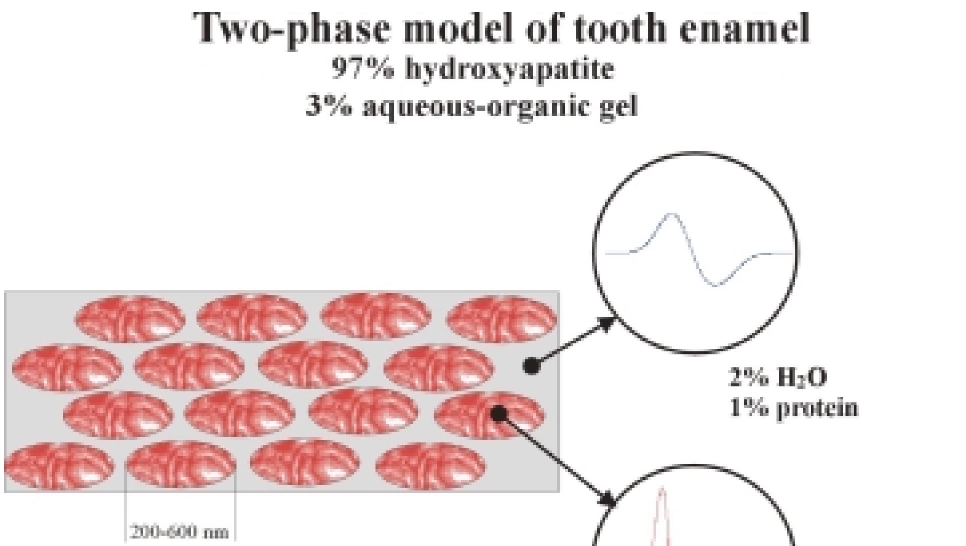




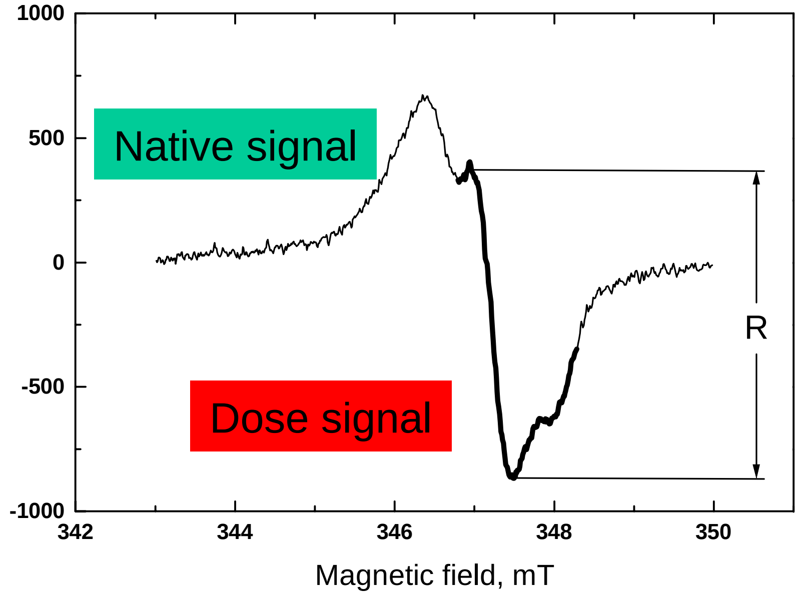
EPR Biodosimetry – Teeth (Fundamentals)

- Carbonate impurities, which are incorporated into or attached to the surface of hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) crystals during formation, are converted to $CO2^-$ radicals through absorption of ionizing radiation.
- Concentration of radicals increases with absorbed dose.
- Intensity of the EPR absorption is a measure of the absorbed dose.

EPR Biodosimetry – Teeth (Fundamentals)



Romanyukha, et. al,
Appl. Radiat. Isot.
(2000)



Why tooth enamel?

- Highest degree of mineralization (97%).
- Stable radiation-induced centers (~10^6 years).
- Linear dose dependence of radiation induced ion concentration.
- Low detection limit (<100 mGy).
- Sensitive to γ-, β-radiation and x-ray.

DOSE RECONSTRUCTION BY THE EPR METHOD
(Teeth)

Protocol — **Considerations**

SAMPLE COLLECTION
Tooth Health

Storage

Location
- UV effects
- metabolism

PREPARATION
Chemical Treatment
- [KOH]
- temperature
- time
- protocol
- ultrasound settings

Crush/Sieve
- particle size

Drying
- temperature
- time

MEASUREMENT
EPR Calibration and Standards
Spectral Parameters
Sample Geometry
Background Signal Subtraction
Radiation SignalMeasurement

DOSE ASSESSMENT
Calibration Curve

Additive Re-irradiation
- irradiation conditions and standards
- calibration design
  - > number of points
  - > dose intervals
  - > dose range
  - > replicate number

DATA ANALYSIS
Response Curve Fitting Routine
Confidence Interval Determination

INTERPRETATION
Tooth Age & Position Corrections
Conversion to Organ Dose

EPR Biodosimetry -Teeth (Protocol)

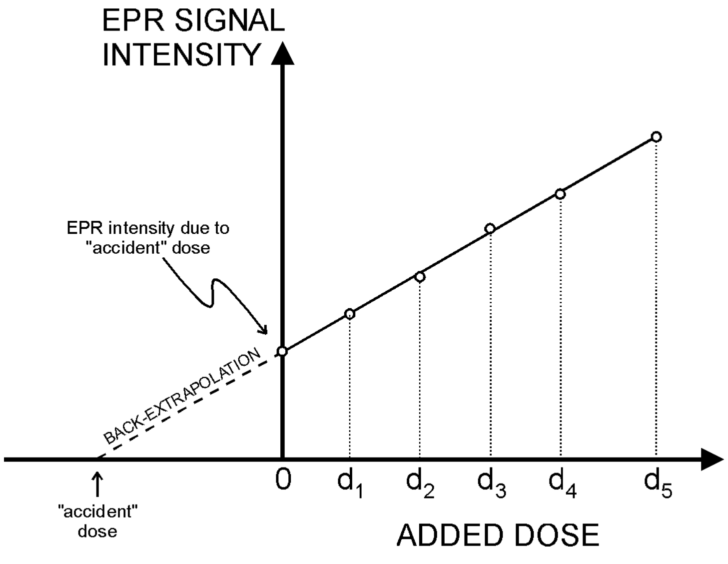
- Sample Collection
    - Dental diseases can change the mineral content and carbonate concentration.
    - Only sound (healthy) part of tooth enamel should be used for analysis.
  - Location
    - Adults have 32 teeth from four different types:
      - Molars (12), premolars (8), canines (4), and incisors (8).
    - UV-induced signal.
      - Should use molars and premolars and the inside of enamel for incisors and canines.

EPR Biodosimetry Fundamentals (Protocol)

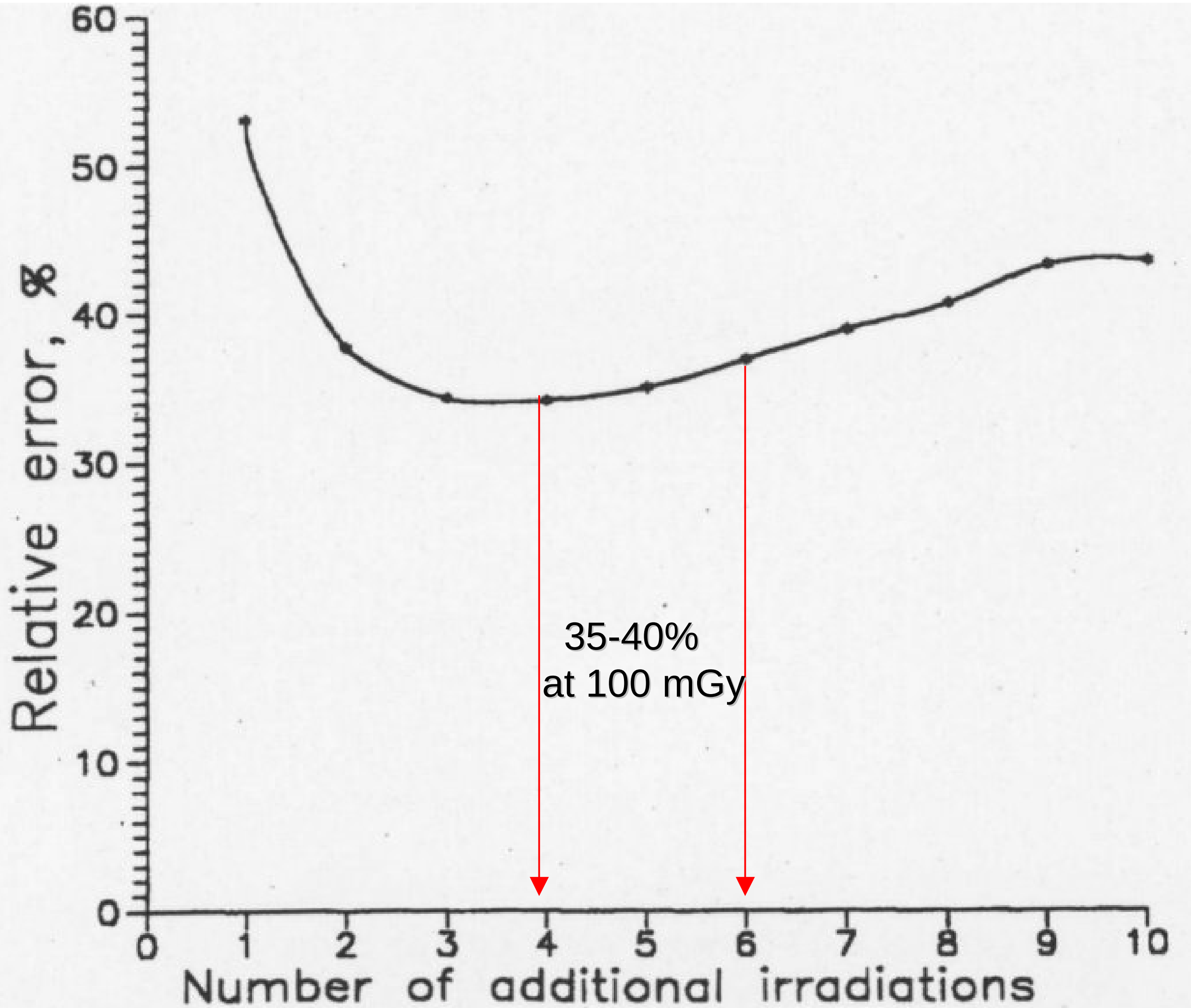
- Sample Preparation (separate dentin from enamel):
  - Mechanical Method
    - Dentin removed by drill & enamel ground into powder.
  - Semi-chemical Method
    - Dentin removed by drill.
    - Monitor removal using fluorescence stimulated by 360 nm UV.
    - Enamel granulated & etched with orthophosphoric acid.
  - Chemical Method
    - Softening & removal of dentin with NaOH or KOH lye in an ultrasonic cleaning unit.
    - Granulate enamel with optional etching of the ground sample.

EPR Biodosimetry Fundamentals (Protocol)

- Dose Assessment (Calibration Methods) - I
  - Individual calibration (additive dose method)
    - Sample is irradiated in the laboratory with several additional doses.
    - Amplitude of the dosimetric signal is measured after each irradiation.
    - Original unknown dose is obtained form the intercept of the linear regression line with the dose axis.



EPR Biodosimetry Fundamentals (Protocol)

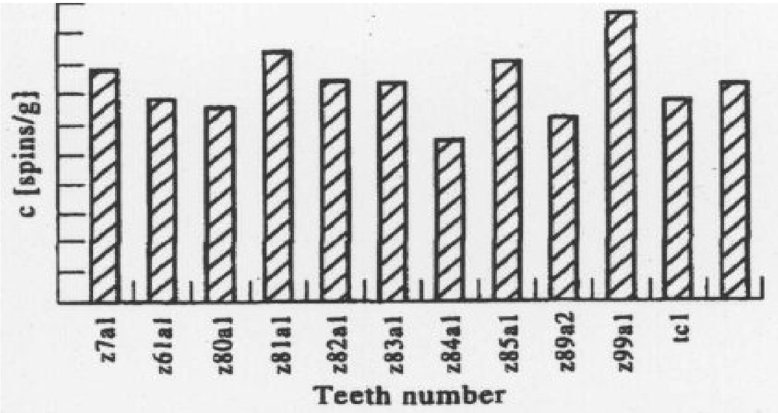


Dependence of relative error of dose determination on number of additional irradiations.

Chumak, *et al*.,
Appl. Radiat. Isot.
(1996)

EPR Biodosimetry Fundamentals (Protocol)

- Dose Assessment (Calibration Methods) – II & III
  - Calibration curve
    - Dose response function of tooth enamel established by *in vitro* irradiation of young adult teeth with negligible external exposure.
    - Assumes moderate variation in radiation sensitivity.
  - Non-destructive calibration
    - Small fraction (15 mg) of the sample is exposed to one large dose to determine its sensitivity.

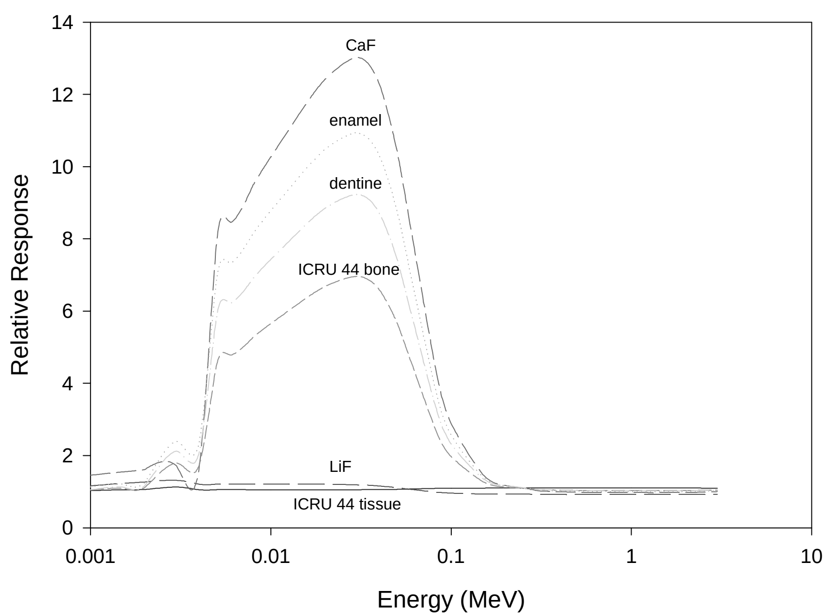


Concentration *c* of CO_2^- in different teeth irradiated with 1.1 Gy and measured with 2 mW.

Egersdorfer, *et al.,* Appl. Radiat. Isot. (1996)

EPR Biodosimetry Fundamentals (Protocol)

- Data Analysis and Interpretation
  - Confidence interval determination
  - Tooth age and position corrections
  - Conversion to organ dose

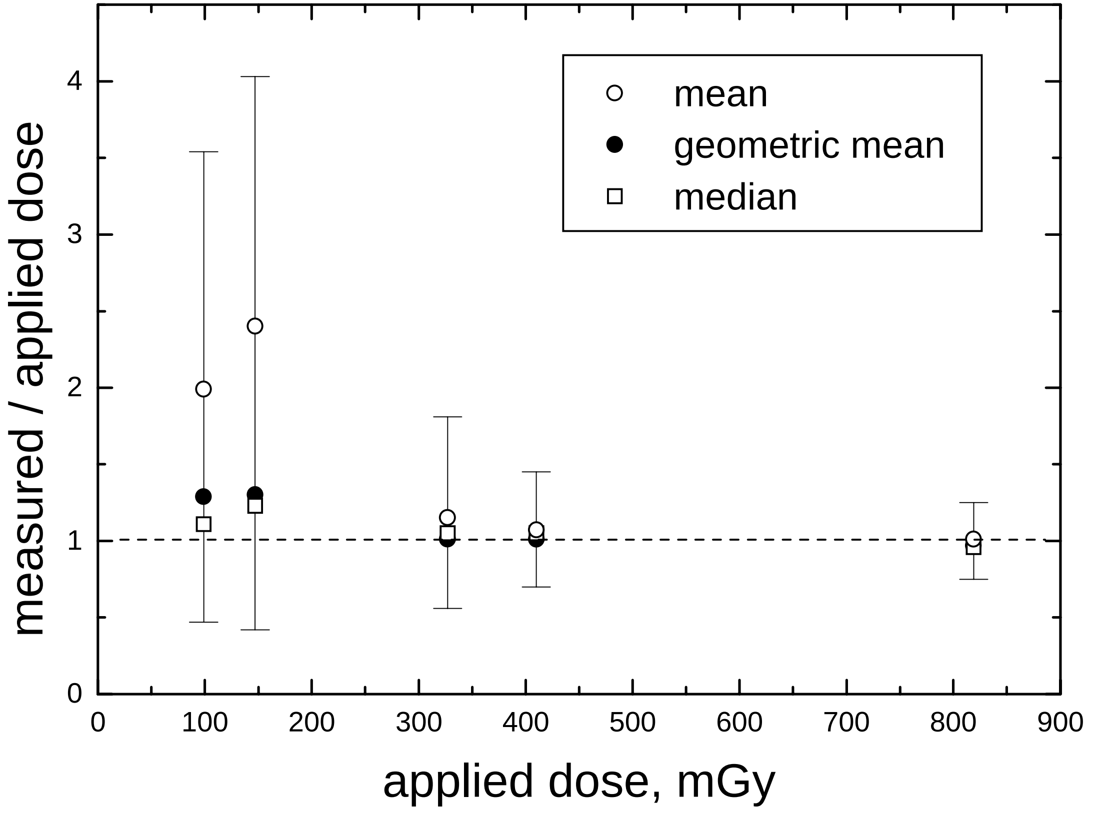


EPR Biodosimetry Fundamentals (Protocol)

- Sources of Errors
  - Imperfect sample preparation techniques.
  - Inequivalence of irradiation conditions of test and reference samples.
  - Inadequate methods of spectrum processing.

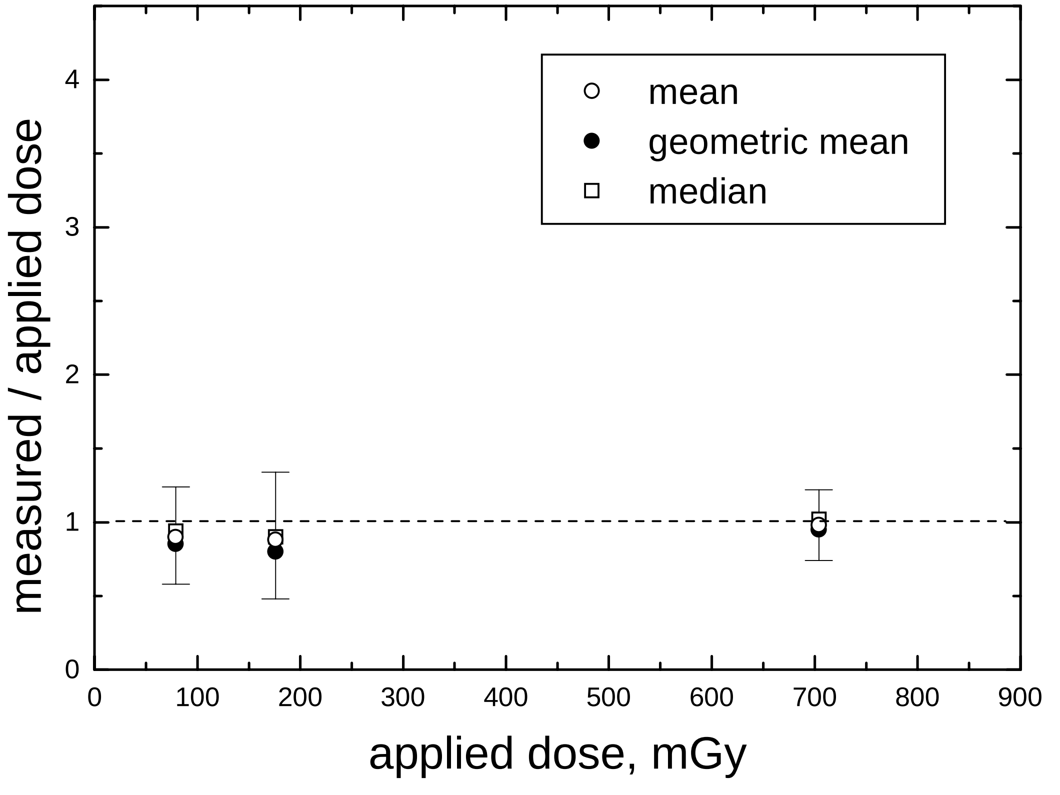
EPR Biodosimetry (Intercomparisons)

2nd International Intercomparison on EPR Tooth Dosimetry
1999, Results of 18 Laboratories



EPR Biodosimetry (Intercomparisons)

3rd International Intercomparison on EPR Tooth Dosimetry
2003, Results of 12 Laboratories



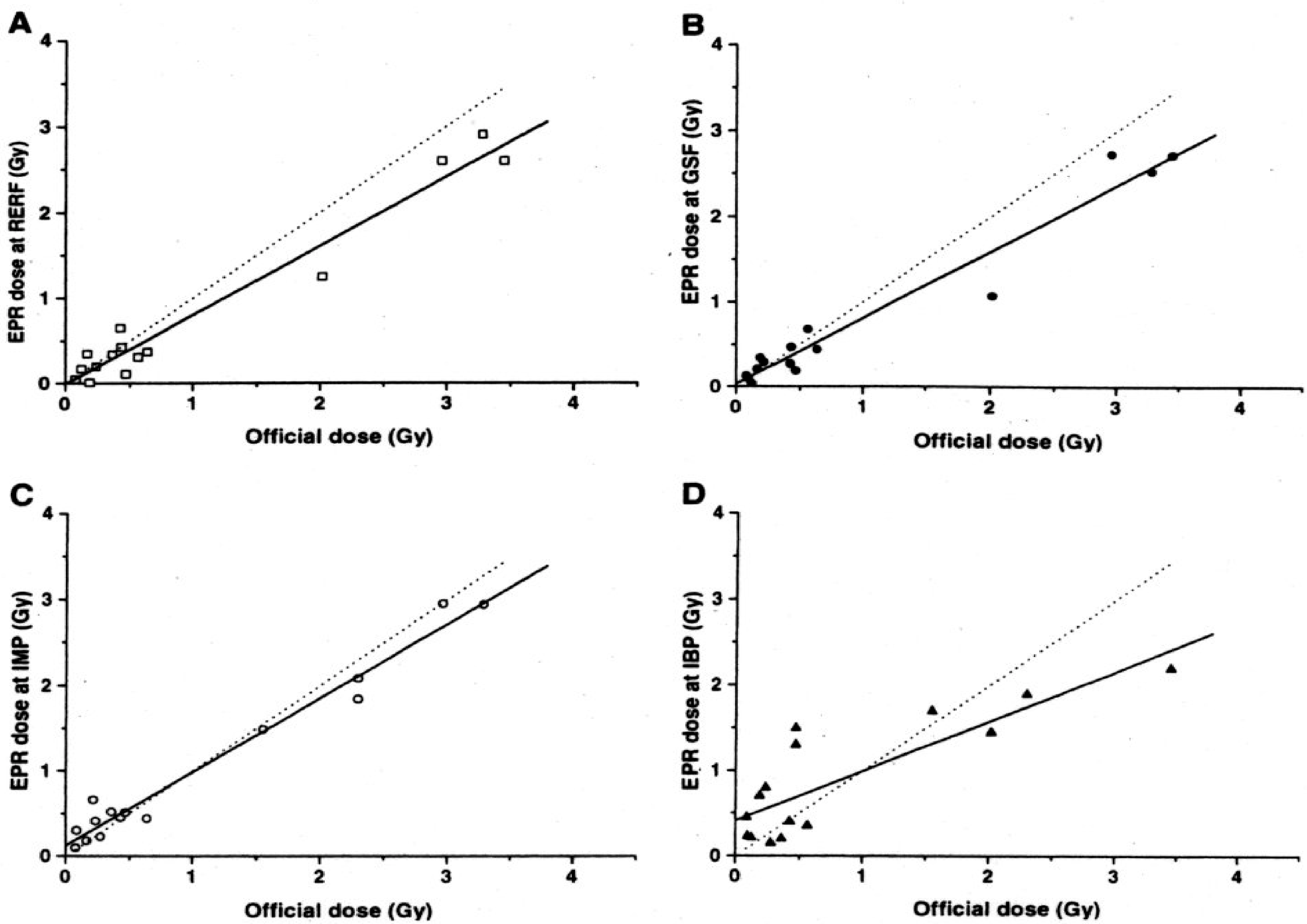
EPR Biodosimetry Applications

(Epidemiological Investigations Using Tooth EPR)

Description of group	**Year of over-exposure**	**Number of reconstructed doses**	**Values of reconstructed doses, Gy**	**Reference**
Survivors of a-bombing of Hiroshima, Japan	1945	100	0.3-4.0 Gy	Nakamura et al., Int. J. Radiat. Biol. 73, 619-627 (1998)
Mayak nuclear workers, Russia	1948-1961	~100	0.2-6.0 Gy	Wieser et al., sub. to Health Phys. Romanyukha et al., Health Phys. 78, 15-20 (2000)
Techa riverside population	1948-1958	~100	0.1-10 Gy	Romanyukha et al., Health Phys., 81, 554-566 (2001) Romanyukha et al., Radiat. Environ. Biophys., 35, 305-310 (1996)
Eye-witnesses of Totskoye nuclear test, Russia	1954	10	0.1-0.4 Gy	Romanyukha et al., Radiat. Prot. Dosim., 86, 53-58 (1999).
Chernobyl clean up workers, Ukraine	1986	660	0 - 2.0 Gy	Chumak et al., Radiat. Prot. Dos. 77, 91-95 (1998)
Population of areas contaminated by Chernobyl fallout, Russia	1986	2500	~ 0.1 Gy	Stepanenko et al., Radiat. Prot. Dos. 77, 101-106 (1998)
Semipalatinsk population	1950s	32	0.3-4.0 Gy	Romanyukha et al., Appl. Mag. Res.., 22, 347-356 (2002)

EPR Biodosimetry – Teeth

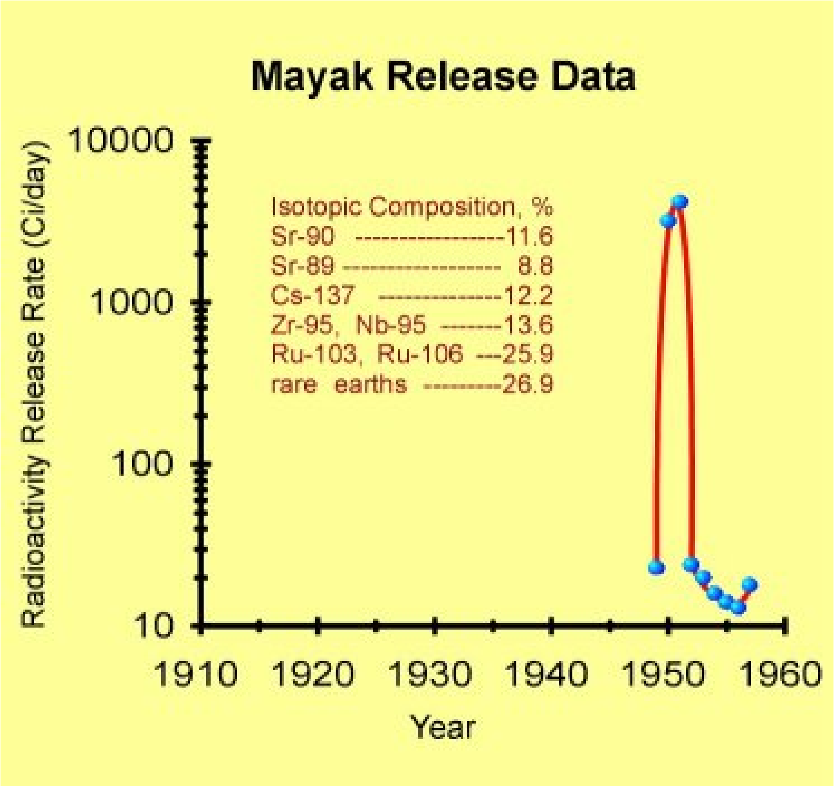
(Russian Nuclear Workers - Mayak)

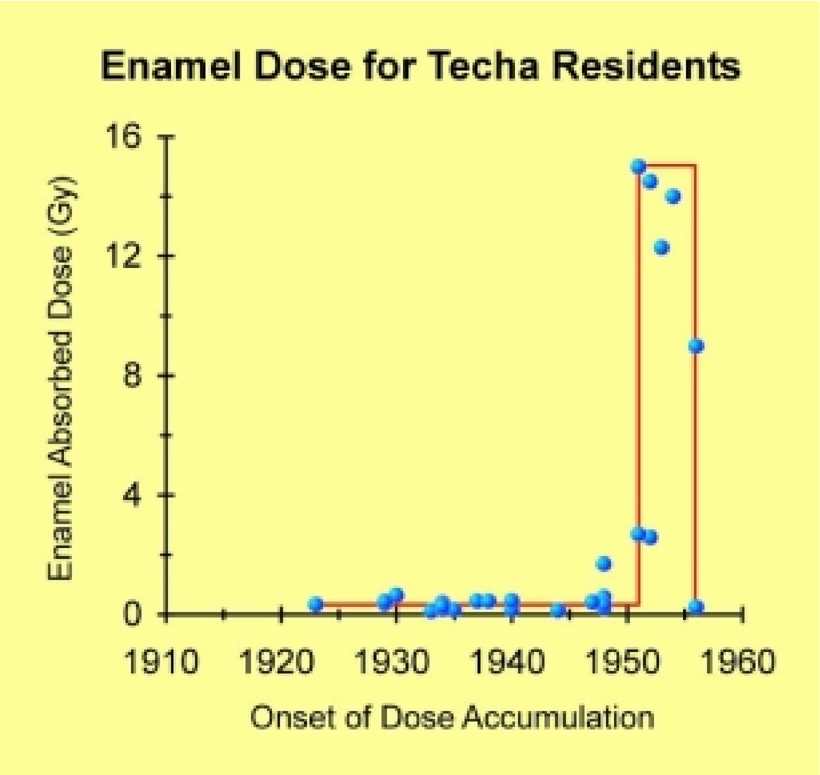


Romanyukha, et. al. (2001)

EPR Biodosimetry - Teeth

(Residents of the Middle and Lower Techa River - Mayak)





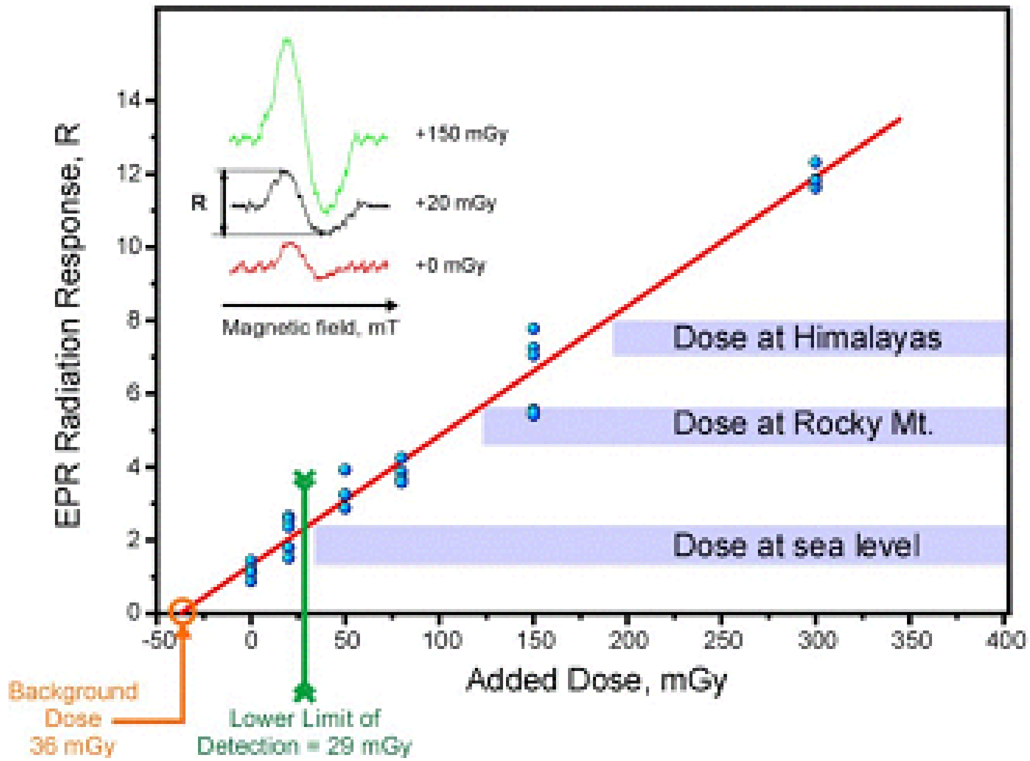
Romanyukha, et. al. (2001)

Issues/Future Development
(EPR Biodosimetry - Teeth)

- Sensitivity (spectral resolution)
- Invasiveness
- Standardization

Issues/Future Development (Sensitivity)

- Lower limit of detection = 29 mGy.
- Equal to US average cumulative dose for a 20 year old due to natural background radiation.



Issues/Future Development (Invasiveness)

- Alternatives to exfoliated/extracted teeth:
  - Q-band (35 GHz)
    - Enamel “biopsy” and tooth restoration (sample size ~35 mg).
  - L-band (1.2 GHz)
    - Non-invasive *in vivo* measurements
      - Sensitivity 50-100 ±25 cGy (preliminary studies)

Issues/Future Development
(Invasiveness)

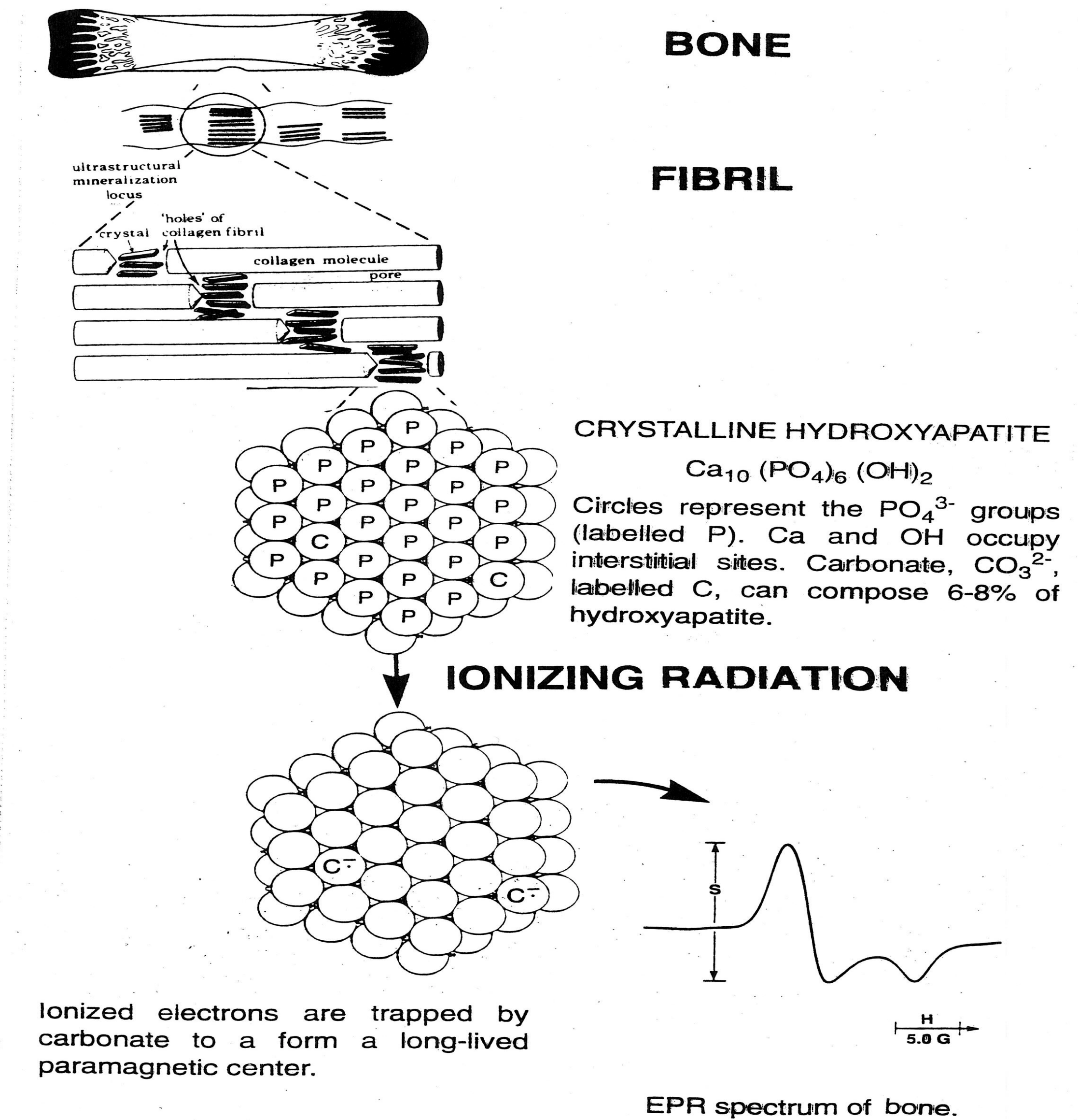
Issues/Future Development (Standardization)

- IAEA-TECDOC-1331 (December 2002), “Use of EPR dosimetry with tooth enamel for retrospective dose assessment”.
- ICRU Report 68 (2002) “Retrospective assessment of exposures to ionising radiation”.

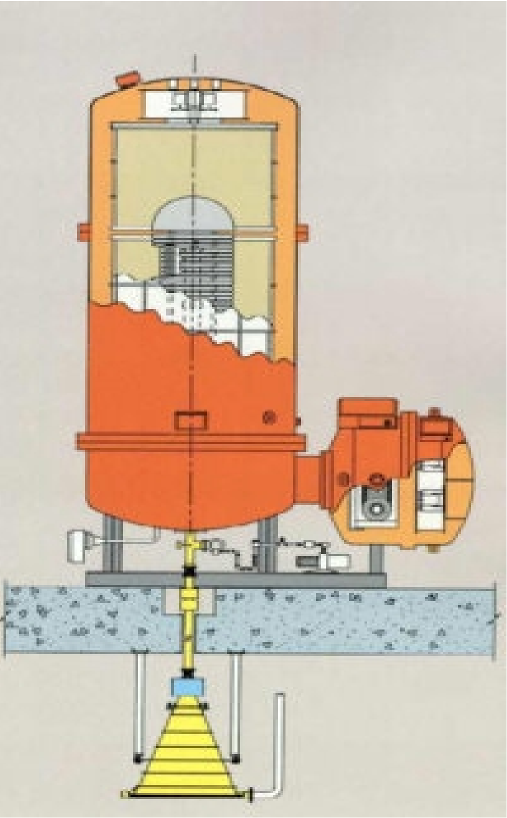
Measurement of	Type of exposure			
	External, gamma [a]	Internal, alpha [a]	Internal, beta [a]	Internal, gamma [a]
EPR of enamel		-		
Chromosome aberrations		-	-	
Micronuclei or mutations		-	-	
Luminescence of ceramics		-	-	-
Radionuclides in human body	-			
Radionuclides in environment				

[a]: Type of radiation field.

EPR Biodosimetry - Bone (Fundamentals)

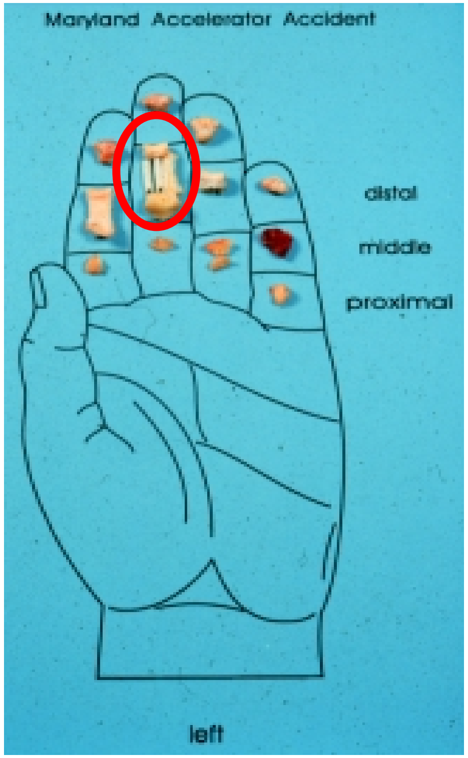


EPR Biodosimetry – Bone
(Applications)

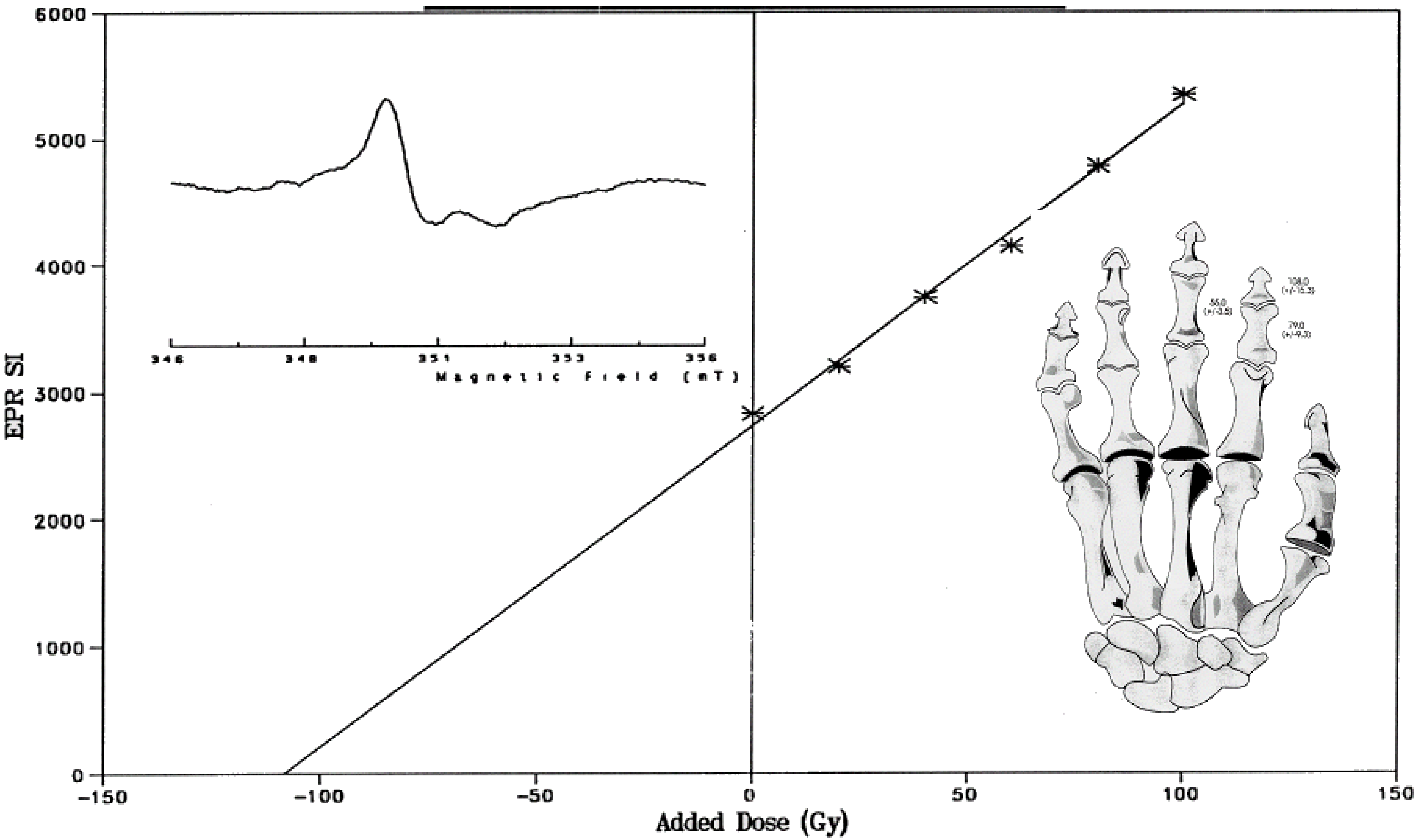


Schauer, *et. al*,
Health Phys.
(1993)

EPR Biodosimetry – Bone (Applications)



EPR Biodosimetry – Bone (Applications)



Conclusions

(EPR Biodosimetry – Teeth)

1. Most versatile biodosimetry method currently available.
   - Recommended by ICRU for individual exposures with largely uniform dose distribution in the human body at a time period of a year to more than a decade after the exposure.
2. Widely applied in epidemiological studies and radiation accidents.
3. Capable of measuring cumulative doses from natural background radiation.
4. Dental enamel may prove useful for portable, non-invasive biodosimetry.