Methodendurchführung wesentliche Vorteile internationaler Kooperationen.

Bei Unfallsituationen können so i. d. R. im eigenen Land, aber auch im europäischen Umfeld Ansprechpartner gefunden werden, die eine optimale Unterstützung des medizinischen Gesundheitsmanagements von Patienten sicherstellen können.

Bei sehr speziellen Untersuchungstechniken mit hoher individueller Expertise sind zudem die Aufgaben außerhalb von Unfällen oder gar Großschadensereignissen immer zu berücksichtigen, damit die Expertise zu jeder Zeit abgerufen werden kann.

Gut ausgebildetes und spezifisch trainiertes Personal, Up-to-date-Geräte und ausreichend Verbrauchsmaterial müssen zur Verfügung stehen, aber auch entsprechende Infrastruktur zur schnellen und effektiven Aktivierung der Netzwerkpartner sowohl im Falle eines Großereignisses als auch bei wenigen potenziell bestrahlten Personen.

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Advantages and Challenges of Using Physical Biodosimetry to Assess Individual Exposure in a Large Scale Unplanned Event

Physical biodosimetry measures the product of a physical phenomenon occurring in the body as a result of exposure to high energy radiation, such as freeing an electron in the chemical make-up of bones, teeth, or nails. This is in contrast both to **physical dosimetry**, which measures radiation-induced changes in objects external to the individual, e. g., in a film badge worn by the individual during exposure, and to **biological biodosimetry**, which measures the body's biological response to ionizing radiation, such as repair cycles in response to resulting injury or the biological product of injury. This review considers the principles and practice of using physical biodosimetry to measure dose to individuals from unplanned radiation exposures.

Potential Value of Physical Biodosimetry

The potential value of physical biodosimetry is analogous to the highly validated and useful dosimetry routinely done with preplaced physical dosimeters such as film badges or ionization chambers, but without requiring preplacement. Instead, like biological biodosimetry, it uses the body itself as the 'dosimeter', so the dosimeter is always in place! Consequently, it has been widely and effectively used, especially in synergy with other techniques, e. g., biological biodosimetry.

Body itself as the "dosimeter"

Because the interactions of ionizing radiation with matter results in the localized deposit of very large packets of energy, potentially any measurable physical change in the body could be used for dosimetry. However, the choice is limited to a few physical/chemical phenomena because, in order to be useful for biodosimetry:

- Radiation-induced changes should be stable over the interval (which can be days or even years) between the person's exposure and its measurement.
- Changes in the body should be unique to radiation and not affected by other sources such as biological mechanisms or the environment such as water or light.
- Signals should be proportionate to dose, i. e., measure the amount of exposure.
- Changes should be measurable by readily applied techniques.

Physical techniques for biodosimetry

These requirements led to using 2 physical techniques for biodosimetry:

- electron paramagnetic resonance (EPR) (also termed electron spin resonance, ESR) and
- optical stimulated luminescence (OSL).

As noted below, because of complications in both techniques for use in large scale unplanned radiation events, only in vivo measurements using EPR of nails and teeth and EPR measurements of isolated teeth are currently being pursued for this use.

EPR Biodosimetry

How EPR Detects Radiation-Induced Products

The measured parameters are radiation-induced unpaired electrons (free radicals) that become stabilized in suit-

Note

Both EPR and OSL techniques, while discussed here for use in physical biodosimetry in large scale unplanned events, are also effective when used to measure dose in incidental inanimate objects on or near the person such as cell phones or foodstuffs, e. g., sugar. Additionally, their same principles may be applied to physical techniques to measure smaller scale disasters and to monitor planned radiation exposures, e. g., radiation therapy or sterilization of foodstuffs. These uses are only briefly reviewed; see especially the following article from page 14.

able components of tissues. Because water impacts the stability of configurations with unpaired electrons, suitable tissues have minimal water content. Within such tissues, radiation-induced unpaired electrons migrate to sites that are energetically most stable.

Teeth, nails, bone and hair

Tissues investigated include teeth, nails, bone, and hair. In teeth, the principal radiation induced EPR signal measured is a carbonate radical anion in the hydroxyapatite matrix. This matrix is especially predominant in the enamel of teeth; therefore, it is where most of the radiation-induced EPR signal resides.

Bone also has considerable hydroxyapatite, but it is less dense than tooth enamel.

Consequently, the EPR signal is not as intense as in teeth. The carbonate radical anion found in irradiated teeth is extremely stable and can persist for many thousands of years. In nails and hair, the location of unpaired electrons is within the keratin (with several sites apparently having similar levels of stability). These sites are not as stable as in the hydroxyapatite matrix; therefore, EPR signals in nails decay over periods of several weeks.

Estimation of the age of historic human finds

The longevity of the carbonate radical anion led to using EPR to date ancient teeth and bones; using background radiation as the source for signals and assuming a constant annual amount, the intensity of the signal is used to estimate their age.

Advantages

The radiation-induced changes in nails, teeth, and bones occur immediately upon exposure and persist. Therefore, measurements can be made at any time starting immediately after the event. (There are a few short-term time-dependent changes in the EPR signals immediately after irradiation, but these are small in magnitude, occur within a few hours of the exposure, and have been well characterized for a long time [1, 2]). Because neither dose rate nor elapsed time affect assessing the magnitude of the overall dose, measurements can be made at any time after the exposure, from immediately up to many weeks for nails, years for bone, and indefinitely for teeth.

Measurements at any time after the exposure

Based on the usual criteria for significant acute effects (e. g., dose ≥ 2 Gy) these methods are fully capable of resolving the doses needed for effective triage [3, 4].

The dose assessed is specific to the site being measured, e. g., to the tooth or to the nail on a specific limb. For this reason, measurements made at different sites on the body, e. g., nails on a hand and foot, can be used to assess whether the exposure is homogeneous or differs by location on the body. This contrasts with biologically based biodosimetry parameters, which typically assess systemic or organ-specific responses to dose and therefore their measurement is indefinite about dose uniformity. Likewise, because it is physically-based and not a biological response to injury, EPR signals are at most minimally confounded by simultaneously occurring factors such as wounds and stress.

Challenges

Some EPR parameters, if not measured in vivo, require invasive sampling such as extracting teeth or biopsying bone. Measurements may not always be possible, e. g., if the person has no teeth. Some techniques may require preparation, e. g., if nails need polish to be removed. If there was significant dose from surface contamination of beta emitters, the tissue dose could be over-estimated. There is a concern that EPR signals from ultraviolet (UV) exposure could be a significant source of error when EPR is used to measure low doses. This has been examined and, although UV exposure can add to background signals in teeth or nails, its contribution is very low compared to the radiation-induced signal. This is due to rapid saturation in the dose-response of the UV signal with exposure time and, given the low penetrance of UV light, confinement of the signal to a very small surface volume of the tooth or nail [5, 6].

Invasive sampling required

Types of EPR Parameters for Biodosimetry

Tooth EPR, measuring isolated enamel

Retrospective studies of radiation exposures in populations from Japan and the USSR, using exfoliated teeth and concentrating the enamel, demonstrated that accurate EPR measurements in irradiated teeth could be made at low doses of radiation (< 0.1 Gy) that were extremely pertinent for radiation epidemiology [7]. Many laboratories use this approach, and today it remains one of the most important methods to understand the long-term consequences of low dose irradiation in human populations. Nevertheless, while tooth biopsies have been used in the absence of having exfoliated teeth, in vitro tooth biodosimetry using biopsies has not been widely considered for triaging victims in large scale events.

In vitro tooth biodosimetry

Tooth EPR, measured in vivo

The great attraction of making EPR measurements of teeth in vivo is that it eliminates the rate-limiting step of extracting or biopsying teeth in order to estimate doses for immediate triage following a large radiation event.

The original attempts to make in vivo tooth measurements were done by **Motoji Ikeya** and colleagues [8], using an X-Band (9 GHz) EPR device. While capable of measuring teeth inside the mouth, it was very awkward to place and hold the resonator on the teeth, and there were significant problems with local heating of tissues due to the high frequency. These in turn produced excessive noise, termed baseline distortion.

Measuring teeth inside the mouth

As low frequency (L-band, 1.2 GHz) EPR began to be established for other purposes, it was natural to investigate using low frequency EPR to measure teeth in vivo, since it could overcome the heating problems of X-Band EPR.

Although it took several years and additional problem-solving to make rapid, sensitive measurements, L-Band EPR in vivo tooth biodosimetry was demonstrated under conditions compatible with its use for both primary and secondary triage in large events [3, 4].

Key developments included:

- Measuring one or both upper front incisors instead of molar teeth (as usually used in in vitro tooth biodosimetry). Incisors were less likely to have caries or repair. Their large flatter surfaces and greater accessibility made resonator placement easier, also allowing the subject to sit, all of which increased the stability of measurements.
- Replacing multiple placements of the resonator during a measurement session with automatically rotating the magnet through several small angles, thus minimizing noise.
- Automating data processing and troubleshooting.
- Designing the magnet specifically to measure incisors. This allowed minimizing its size and weight, while fitting more than 95 % of individuals.
- Making an ergonomically robust structure for the spectrometer that could be operated by novice operators after only a few minutes of training.

Fully automated and compact designs have been developed, and a readily transportable version has been made.

Presently L-band EPR in vivo tooth biodosimetry can measure dose +/– 0.5 Gy within < 5 min. data acquisition [4, 9].

Dose +/– 0.5 Gy within < 5 min. data acquisition

The system is capable of being operated by previously naive operators with < 15 min. training.

A prototype of this version was successfully deployed to Japan, where it was transported to the Prefecture of Fukushima to make retrospective measurements of people living in the region at the time of the 2011 nuclear power plant accident [10].

This device seems suitable for use in a large radiation event for both first and second stage triage.

Initially designed to meet US specifications for primary triage of up to 1 million being assayed in the field within 6 days [11], it may be especially valuable for secondary triage. In this scenario, in a more controlled environment, high transportability would not be essential and higher quality EPR biodosimetry assessments can be made of victims already identified as at risk of acute radiation syndrome (ARS), using operators with modest just-in-time instruction. The site-specific nature of EPR physical measurements of the tooth could be used in conjunction with other types of biodosimetry to determine whether the dose was homogeneous or not.

Risk of acute radiation syndrome

Nail EPR, using clippings

Initial findings using EPR measurements of clippings from human fingernails were very promising. As early as 1968, an EPR signal was observed in nails irradiated at 40 Gy in vitro at 20 °C, and it the technique appeared to be able to detect much smaller doses [2].

Because of the ease of obtaining nail clippings (even allowing self-sampling) and their distribution throughout the body at 4 different limbs, there has been great interest in their use as biodosimeters. Clippings could even be examined at a remote site using very sensitive (higher frequency) EPR instruments and expert operators.

Unfortunately, it soon became apparent that the situation was quite complex. Recent investigations carried out by many scientists found numerous problems compromising the use of nail clippings for triage after a large-scale event. Problems include the presence of background signals in the nails that mask or distort radiation induced signals (RIS); induction of very large and complex EPR signals from cutting nails (referred to as mechanically induced signals (MIS)) that mimic RIS); a complex set of RIS which, together with MIS and background, have very complex patterns of decay and regeneration impacted by many factors including hydration, oxygen, and drying [12]. Other complications with nails present challenges as well, including polish or other cosmetic treatments of nails and occupational or environmental exposures such as UV.

Recent investigations

Although clipped nails are no longer considered a likely biodosimeter for triage, clipped nail biodosimetry plays an important role in events with high doses (> 10 Gy) and involving only a few individuals. For example, very useful results were obtained to estimate high doses received by several workers who handled ^{192}Ir radioactive sources used in radiography cameras in Tunisia, Gabon, and Peru [13].

Nail EPR, measured in vivo

As noted above, using nails as biodosimeters can potentially provide critically needed information on the homogeneity of the radiation exposure. Being able to make independent, site-specific measurements at multiple locations on the body provides a unique capability to determine whether there may be sufficient volume of bone marrow to overcome radiation injury to the hematopoietic system, obviating the need for extreme life-saving and scarce medical interventions such as bone marrow transplantation.

Homogeneity of the radiation exposure

Consequently, after discovering the great complexities in using nail clippings for EPR biodosimetry on a large scale, interest was renewed in making measurements of nails in vivo to avoid the complexities introduced when clipping and handling nails. Nevertheless, the in vivo solution used for teeth, i. e., switching to low frequency L-band to avoid the problem of non-resonant absorption of the microwave by water in the tissues, was not viable because the RIS EPR signal in nails is of too low an intensity and too complex to use L-band. To solve this dilemma, reasoning that the nail itself has a low water content (although not so the underlying nail bed), a systematic search was made for resonant structures that would be able to make measurements in a very limited thickness, i. e., restricted to the nail, avoiding the lossy structures of the nailbed. This could allow safe use of higher frequency EPR to measure RIS in vivo in nails.

Measurements in a very limited thickness

2 resonator geometries, the aperture resonator [14] and the surface array resonator (SRA) [15], exhibited these desirable characteristics. The SRA has proven to be more amenable to systematic improvements and, because of excellent progress in its sensitivity [12], it is the resonator used in current studies of nails in vivo. Furthermore, sensitivity of the measurement can be very significantly increased as needed by assessing several digits per limb.

Conclusion

EPR biodosimetry of exfoliated teeth is an important part of studies to determine long term consequences of exposure to ionizing radiation. Fully developed, in vivo nail biodosimetry as well as in vivo tooth biodosimetry could become very important and useful components of the immediate response to a large radiation event. It could inform medical response by providing the most important information needed about external exposures, i. e., the magnitude of each individual's dose and whether it was homogeneous.

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