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High Energy Photon Dosimetry by ESR Spectroscopy in Radiotherapy

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Abstract. The finding of long lived free radicals produced by ionizing radiation in organic crystals and the quantification of this effect by electron spin resonance(ESR) spactroscopy has proven excellent dosimetric applicability. The tissue equivalent alanine dosimeter also appear appropriate for radiation therapy level dosimetry. The dose measurement was performed in a Rando phantom using high energy photons as produced by high energy medical linear accelerator and cobalt-60 teletherapy unit. The absorbed dose range of the ESR/alanine dosimetry system could be extended down to 0.1 Gy. The response of the alanine dosimeters was determined for photons at different therapeutic dose levels from less than 0.1 Gy to 100 Gy and the depth dose measurements were carried out for photon energies of 1.25MeV, 6 and 10 MV with alanine dosimeters in Rando phantom. Comparisons between ESR/alanine in a Rando phantom and ion chamber in a water phantom were made performing depth dose measurements to examine the agreement of both methods under field conditions.

Introduction

It is very important to measuring absorbed dose and dose distribution in tissue for high energy photon beam from medical linear accelerator. Present practice at most centers with high energy accelerators are to use an ionization chamber which is calibrated as an exposure meter for cobalt-60 gamma ray and evaluate the absorbed dose in water phantom at the position of the ion chamber.

The absorbed dose is very difficult to measured directly on the interesting points in medium with gas filled ion chambers.

For the convertion of exposure into absorbed dose at an arbitrary point in the phantom, some information is needed on the energy and angular distribution of the photon at the place of measurement, on the stopping powers of the different materials involved on the displacement of the effective point of measurment and field perturbation by the ion chamber.

By contrast, the dosimetry method described here uses solid organic compounds, particularly amino acids that radiation induced reactions in biological molecules rather than in inorganic substances are closer to the radiation effects in living tissue.

A biologically important and quantitatively accessible radiation effect in organic substances

is the production of free radicals. Free radicals in crystalline biomolecules are relatively stable intermediate products of a sequence of events, which, as in tissue, are started by the initial absorption of radiation energy.

Quantitative analysis of the free radicals may therefore be biologically relevant dosimetry, particularly since the free radicals are key intermediates in the processes leading to biological damage of cellular components. Alanine dosimeters may be considered tissue equivalent so that the uncertainty in the mean stopping power ratios of water to the alanine and paraffin mixture are very small.

The dosimeters are assumed to disturb neither the flux of the primary photon beam nor of the secondary particles. Since alanine dosimeter can be inserted directly into the phantom, wall effects must not be considered.

It was the aim of the present study to check for these expectations and to evaluate the applicability of the ESR/alanine system for precise phantom dosimetry of high energy photon beam.

Materials and methods

The radiation measurement technique of free radical dosimetry is based on the quantitative evaluation of radiation induced free radicals by electron spin resonance(ESR).

ESR can be defined as resonant absorption of electromagnetic energy in paramagnetic substances by transition of the spin of an unpaired electron between different energy levels, in the presence of a magnetic field. For an unpaired electon in a magnetic field, two energy levels E1 and E2 exist. The energy difference $\triangle E$ between these levels is proportional to the Lande factor g, the Bohr magneton μ_B, and the magnetic flux density H. The Lande factor is dimensionless and depends on the total angular momentum of the electron. The relationship is given by the equation.

$$E_2 - E_1 = \triangle E = \mu_B \quad gH \cdots\cdots (1)$$

In the ESR spectrometer, the microwave field is generated with a klystron, which by a waveguide system is coupled to the cavity. The measurement cell holding of the sample is positioned in a magnetic field of high homogeneity, The magnetic field is scanned linearly and in addition is modulated by an RF field.

For the resonance condition, the absorbed energy from the sample will change the balance of the microwave system. Normally, the first derivative of the absorption curve is registered by an XY recorder as a function of the magnetic field, yielding the typical ESR spectrum.

Amino acids belong to a class of biological substances, which after irradiation exhibit still reasonably well resolved spectra. Amino acids are components of proteins that can be purified in crystalline form and single crystals are a prerequisite for reliable identification of free radicals by ESR spectrometry.

The application of amino acids to a successful and versatile free radical method of dosime-

try depends on the magnitude of redical yield per unit absorbed dose and on the life time of the radicals. Crystalline alanine fulfills these criteria.

Alanine is an amino acid of the type

$$CH_3 - CH - COOH$$
$$\quad\quad\quad |$$
$$\quad\quad NH_2$$

Among the radical species generated by irradiation, the radical

$$CH_3 - \dot{C}H - COOH$$

is predominant at room temperature.

The three methyl protons of this final fragment are interchanging rapidly by rotation or tunnelling and are magnetically equivalent at room temperature.

Figure 1 shows the first derivatives of the paramagnetic absorption spectrum of alanine sample irradiated at 10Gy dose level, as supplied by the routine readout procedure. The ESR spectrum consists of several lines(hyperfine structure) caused by the hyperfine interaction of the unpaired electron with H-nuclei. Representative of a given dose is the spin concentration which can be determined from the ESR spectrum by appropriate analysis.

For dosimetry the signal to dose conversion does not necessarily provide values of absolute spin concentrations directly, but such values can be derived from measurements of relative ESR signals.

In the structure of ESR spectrum for doses, the peak to peak value(in arbitrary units, e. g. millimeters) of the ESR spectrum is a representative dosimetric reading. It is evident that the specific gain factor of the ESR spectrometer has to be taken into account for quantitative considerations.

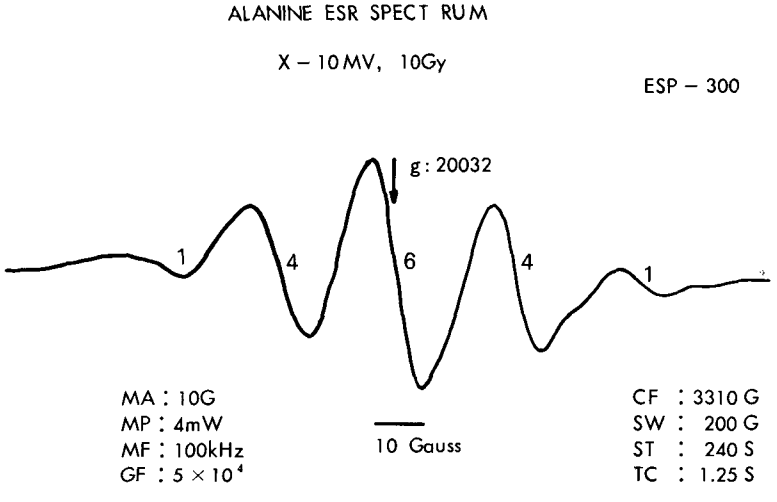

Fig. 1. ESR spectral shape of alanine dosimeter irradiated 10Gy of 10 MV x-ray

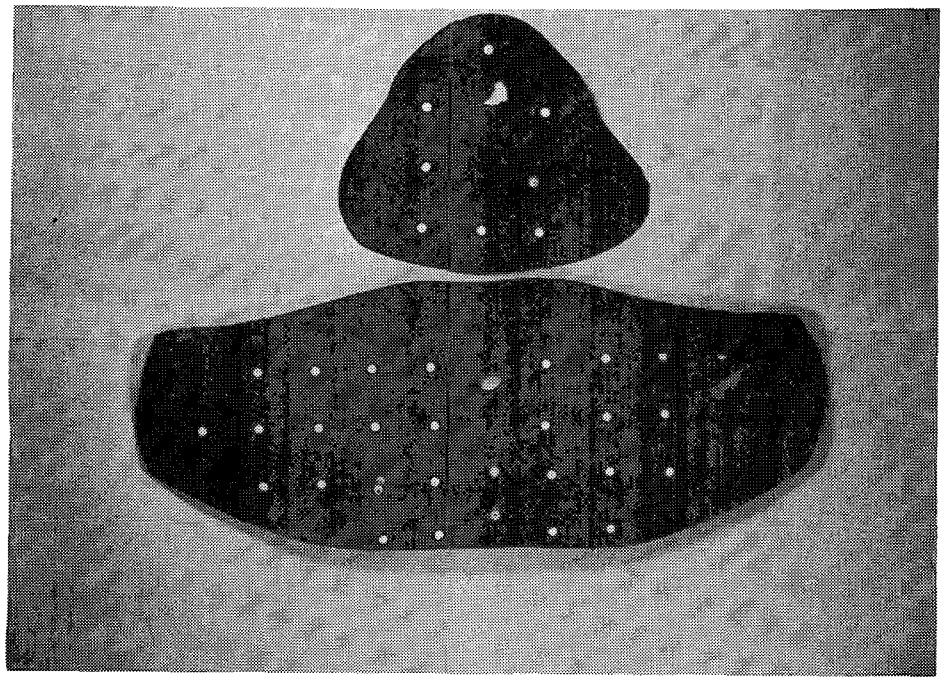

Fig. 2. Alanine dosimeters of inserted into a humanoid phantom

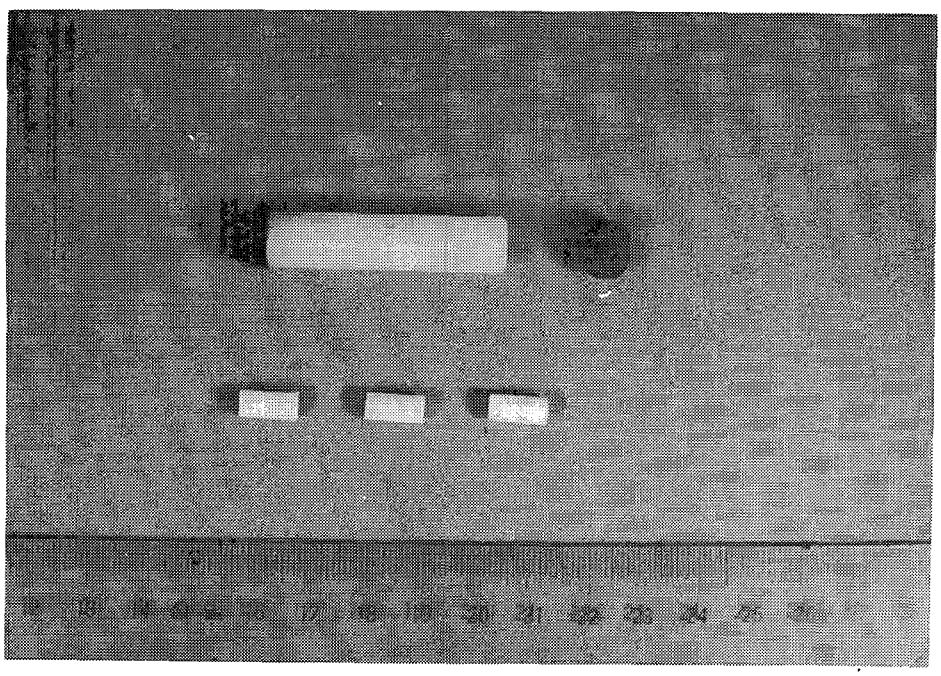

Fig. 3. Alanine dosimeters and build up holder capsule

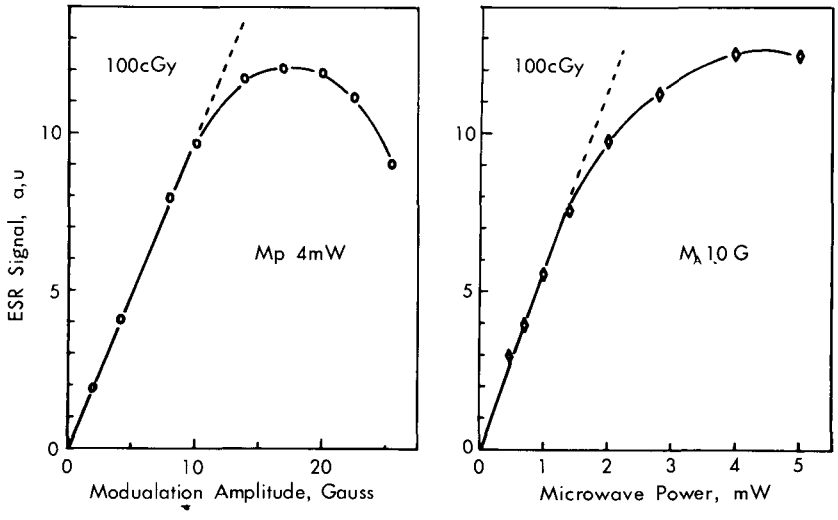

Fig. 4. ESR signal amplitudes for microwave power and modulation amplitudes

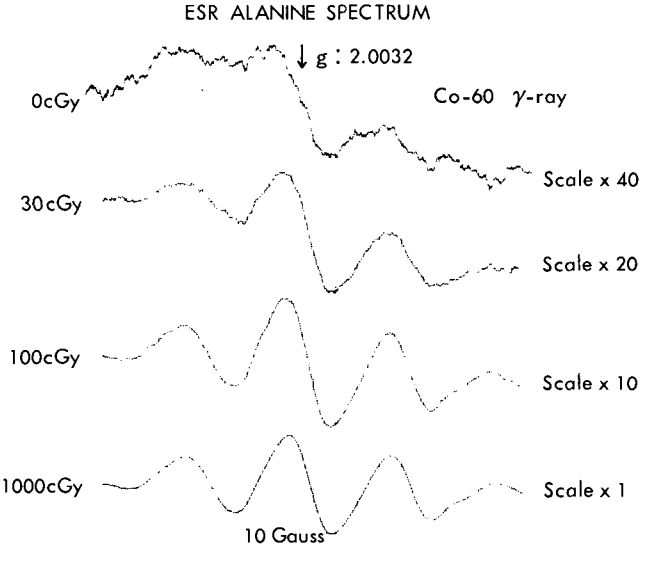

Fig. 5. Alanine/ESR spectrum for absorbed doses of cobalt-60 gamma ray.

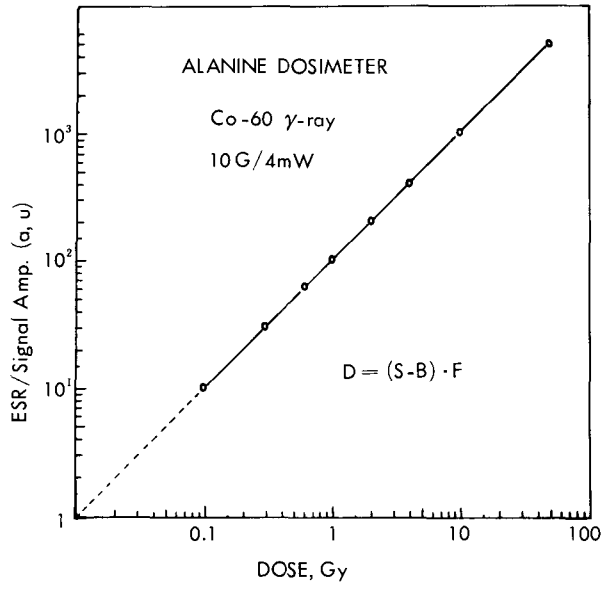

Fig. 6. Linear increase of the alanine ESR signal with absorbed dose.

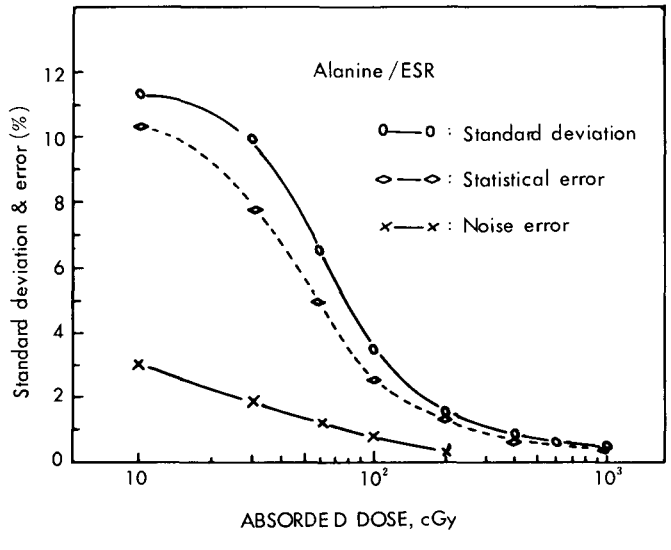

Fig. 7. The relative standard deviation and error of the presently used alanine dosim eters.

The photon beams were performed at a medical linear accelerator and cobalt-60 teletherapy unit. The measuring quantity was the absorbed dose in phantom. The reference doses at the maximum build up region were determined on the basis of exposure measurements and the use of tabulated conversion factors, considering the respective photon energy. A reference ionization chamber was used, type Capintec I, to measured absorbed dose in the phantom. For measurement of depth dose, a Rando phantom was used for alanine dosimeters to be inserted into the holes in it(Fig. 2).

Alanine samples for the ESR/alanine dosimetry were made on the basis of crystalline alanine with an admixture of 20% paraffin. For calibration of the ESR/alanine dosimeters, a standard field of cobalt-60 gamma radiation was used, with a field size of $10\times10cm^2$. The alanine samples are cylindrical shape, 5mm diameter and 10mm in length. For irradiation three alanine dosimeters were inserted into the 6mm$\varnothing$ × 4cm perspex holder replacing the ion chamber position.(Fig.3).

Prior to the photon beam measurements, the detection threshold of the ESR/alanine dosimetry system had to be decreased to a significantly lower dose level than that applied at therapy sessions. Advantage was taken from the availability of a low noise computer aided ESR spectrometer(Bruker ESP 300) operating in the X-band microwave range.

The ESR spectra of the irradiated alanine samples were the first derivatives of the paramagnetic absorption spectra. The spectra were measured within a scan range of 25G with a magnetic field modulation amplitude of 10 Gauss, a microwave power of 4 mW and a time constant of 640 ms(Fig. 4).

For measurement, the alanine samples were inserted into a special quartz tube fitting into the microwave cavity of the ESR spectrometer. All ESR measurements were performed at room temperature. To compare with the ionometric dose measurements, the mean value of the three alanine readings was taken.

Result

1. Dose effect curve

The ESR/alanine spectra of doses from 0 Gy to 10 Gy shown in figure 5 and the response of the ESR/alanine system was covered for therapeutic radiation dose levels. The responses were found to be constant over the entire dose range investigated, i. e. there is a linear dose effect relationship from 0.1 Gy to 100Gy, after substraction of the background signal as measured in unirradiated dosimeters(Fig. 6).

Numerically the ESR/alanine doses were found to be in good agreement with the ionometrically achieved doses for gamma ray from cobalt-60 and 10 MV x-ray from linear accelerator.

The alanine dosimeters evaluated on the ESR spectrometer allowed for a detection threshold of about 0.1 Gy. The threshold was revealed to be determined by the intrinsic ESR signal of the alanine dosimeters and not by the spectrometer noise. Interspecimen scattering at 0.1 Gy was characterized by a coefficient of variation of about 10% and its fluctuations are caused

by reproducibility of readout geometry of the sample and stability of the lower detection limit of the method. The ESR signal increases linearly with dose up to 100Gy, over this dose range, the ESR system can be calibrated in terms of absorbed dose with a single standard sample. The dose reliability of alanine dosimeter was 2%(standard deviation) at 2 Gy dose and decreased to 1% error above 4 Gy photon(Fig. 7).

2. *Energy and dose rate response*

Due to the low effective atomic number, the calibration factor of alanine samples varies only slightly with photon energy relative to the response in biological tissues.

Figure 8 shows the experimentally determined photon energy dependence of ESR response normalized to cobalt-60 gamma radiation. The energy response of 6, 10 MV x-ray and cobalt-60 gamma ray are essentially flat.

The influence of dose rate on the free radical production was studied for cobalt-60 gamma radiation. No variation in response was found between 0.5 Gy/hr and 5 Gy/hr.

3. *Depth dose and dose distribution*

One of the most important for dose planning on radiothrapy is the depth doses to depend

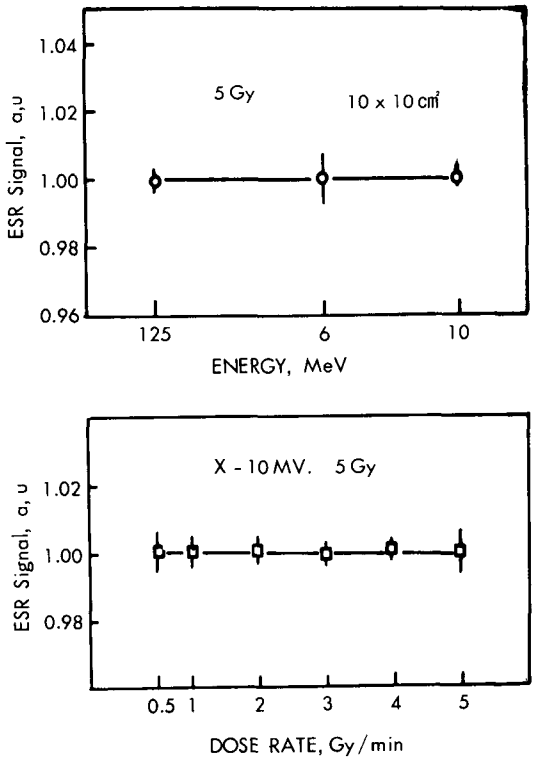

Fig. 8. The dependance of ESR signal of alanine dosimeter for irradiated dose rates and photon energies

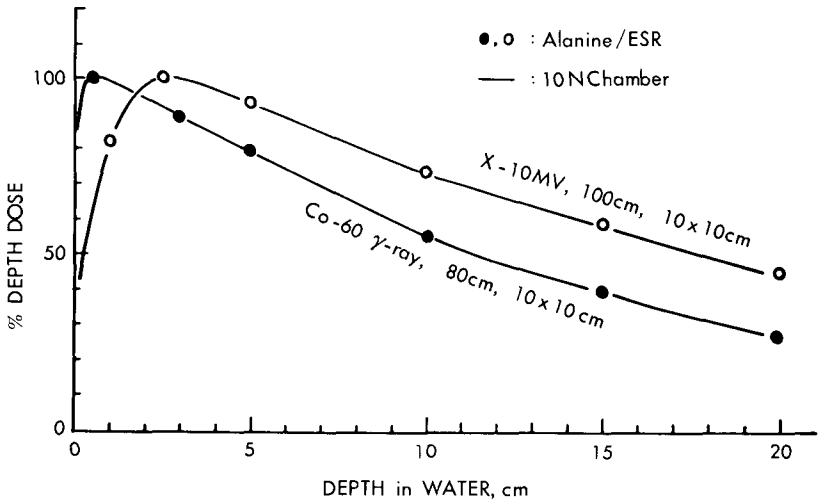

Fig. 9. Comparison of relative depth dose as measured with ionization chamber and alanine dosimeters for 6, 10 MV x-ray and cobalt-60 gamma ray.

on the photon energy, distance from source to skin and field sizes.

The ion chamber is difficult to dosimetry in side of body, but alanine dosimeter could be inserted on interesting point in body due to small dimention(5㎜×10㎜).

Especially being tissue equivalent meterial(density:1.2, atomic number per mass number:0.546), attenuation and scattering of radiation almost same response as tissue, and it can be measured directly absorbed dose in tissue. Relative depth dose measured with the ionization chamber in water phantom and the dose distributions using alanine dosimeters were were measured inside of Rando humanoidal phanton, the relative absorbed depth doses as achieved iononeetrically and by ESR/alanine dosimetry are compared. At increasing depths, the measured and calculated doses are in good agreement(Fig. 9).

4. *Storage conditions*

The free radical species under consideration were found to have long term stability at room temperature. This was verified by our own measurements over a period of 24 months. During this time the radical concentration of samples stored at 6℃ remained constant to within 1%. The free radicals are stable within 5% at 50°C storage temperature and intermediate relative humidity(40−60%), even for extended storage periods up to two months. Under these conditions, the degree of instability is not affected by the absorbed dose level.

In addition to environmental effects, light, particularly ultraviolet light, tends to affect the dose interpretation of most solid state dosimeters, but the free radicals of alanine dosimter exposured in normal laboratory illuminance levels do not influense ESR signal, even over 4 weeks exposure.

Discussion

Traditional methods of dosimetry have been based on radiation effects in inorganic substances. Typical examples are ionization in air(ion dosimetry), deposition of heat in carbon and metals (calorimetry), discoloration of ferrous sulphate solution(Frike dosimetry), and luminescence in solids(thermoluminescence dosimetry). By contrast, the dosimetry method described here uses solid organic compounds, particularly amino acids that radiation induced reactions in biological molecules rather than in inorganic substances are closer to the radiation effects in living tissue.

Free radical dosimetry(FRD) based on ESR analysis, initially developed for intralaboratory use, has recently reached a status for applications of interlaboratory dosimentry intercomparisons. It may even replace some of the currently used reference methods, e. g. Frike dosimetry, for reasons of sufficient radical stability and systen precision. For the moment, the main limitation is the relatively high cost of suitable ESR spectrometers.

Numerous studies have been made of free radicals in x-and gamma ray irradiated crystalline organic substances. Among them amino acids proved to be particulary suitable for dosimetry. The radical concentration cam be quantified by electron spin resonance measurements. On the basis of quantifing ESR spectral signals, a metrology for high level dosimetry in the range between 1 Gy and 100 Gy has been developed.

FRD using ESR analysis of radiation induced free radicals in alanine is promising for many applications of radiation dosimetry. It combines high accuracy and reliability with a small, rugged, and low price detector that is relatively insensitive to ambient physical parameters and handling.

Contrary to most other solid state techniques, a primary radiation effect in a biological medium is used to determine the radiation dose. No readout treatment of the detectors is needed as in the cases of thermoluminescent dosimeter or lyoluminescence. The new method gives reliable tissue equvalent dose readings, and the ESR signal readout is nondestructive, allowing for repeated evaluations. It is this repeatability of evaluation together with the relatively broad dose range and low overall uncertainty, which gives the ESR readout technique advantage over such methods of free radical dosimetry as lyoluminescence. Alanine responds linearly over a wide dose range to ionizing photons.

Because of its reliable dosimetric properties, free radical ESR dosimetry is suitable for many applications. Although a sophisticated and expensive ESR spectrometer is required, the main future of this dosimetry technique probably lies in large volume reference dosimetry. It is very useful to apply ESR dosimetry for the radiotherapy fields. This study have proven applicability of the ESR/alanine dosimetry system for therapy level photon dosimetry.

The results demonstrate the ESR/alanine system to be rather advantageous for dosimetry in radiotherapeutic dose range from 0.1 Gy to 100 Gy. Apart from the qualified dosimetric properties the dosimeter itself is almost tissue equivalent in atomic number and specific gravity. The concentration of the free radicals is not affected by the spectrometric measurement and can be determined repeatedly. Due to the long life time of the free radicals the dosimeter

can be stored for integrating the entire treatment dose of a patient or for long term documentation of the patient dose.

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-국문초록-

ESR Spectroscopy에 의한 치료용 고에너지 광자선의 선량측정

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방사선치료에 가장 널리 사용하고 있는 Co-60 감마선과 6, 10 MV X-선등 다양한 에너지와 2 Gy 에서 10 Gy의 조사선량 범위에 대한 정확한 선량측정은 방사선치료효과를 더욱 높힐수 있고 휴유증에 대한 선량평가에 도움을 줄 수 있다.

지금까지 방사선치료 범위에 속하는 방사선 계측은 주로 전리함을 사용하였으며 Build up cap 이나 팬텀을 이용하여 노출선량을 계측하고 계측된 값에 에너지에 따른 흡수선량 변환계수, 측정기의 구성물질에 대한 저지능등 많은 변수를 고려해야하는 복잡성이 있으며 인체내의 선량분포측정이 어려웠다.

본실험에 사용한 Alanine 측정기는 아미노산의 일종인 유기물질로서 인체조직과 등가이고 부피가 작으므로 (0.5×1㎝)조직내에 많이 삽입하여 방사선을 동시에 측정할 수 있었다.

방사선에 노출된 Alanine은 구성분자의 일부분이 전리되어 장기간 Free radical 상태로 존재하며 마이크로파를 투과시키면 전자의 고유진동수와 일치된 전파를 흡수하는 전자스핀공명(Electron spin resonance)이 일어나고 흡수된 전파의 강도를 측정함으로서 흡수선량을 추측할 수 있다.

방사선흡수선량 측정은 Co-60 원격치료장치의 선원에서 80㎝ 거리에 3개의 Alanine 측정기를 Build up holder 에 넣어 고정시키고 방사선치료 선량범위인 0.1 Gy 에서 100 Gy 까지 조사하였으며 이때 ESR Spectra의 진폭은 흡수선량에 비례하였고 선량 균일성의 표준편차는 2 Gy 에서 1%이었으며 4 Gy 이상에서는 0.5%이었다.

조직내 선량분포를 측정하기 위하여 인체구성과 같은 Rando phantom 내에 Alanine 측정기를 삽입하고 조사면과 에너지에 따른 방사선 흡수선량분포및 심부율을 측정한 결과 표준심부율과 일치하였다.

특히 Alanine 측정기는 온도 습도에 대한 변화가 적고 시간 경과에 대한 변화도 거의 없었으며(년간 약 1% 감소)에너지에 따른 변화도 없었기 때문에 치료방사선 영역의 선량측정과 조직내 선량분포에 적당한 것으로 생각된다.