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Study on the Role of Gold Nanoparticles on External Beam Radiation Using Fricke Gel

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Abstract:- The past decade has seen the emergence of a new radical and ground breaking area of research known as cancer nanotechnology. Using this technology, nanoparticles are being developed in the size range of 1-250 nm and loaded with drugs, imaging agents and genetic materials for improved chemotherapeutic action.

In this work, we have developed XO infused Fricke gel dosimetry and tested the effect of radiation enhancement in the presence of AuNPs. The radiation therapy involves the use of both high energy (MV) and low energy radiation (kV). The results of this work clearly show that in the presence of AuNPs, there can be a great impact on the absorbed radiation and thereby increases the killing efficacy of the cancer cell due to radiation. The use of AuNPs in radiation enhancement and dosimetry planning using Fricke gel has not been reported in the literature. Hence, the finding of this research work is novel and has potential to change the way cancer is currently being treated.

I. INTRODUCTION

Radiation therapy uses high energy radiation to shrink tumours and kill cancer cells. X-rays, gamma rays, and charged particles are types of radiation used for cancer treatment. Radiation is one of the most common treatments for cancer. Other names for radiation treatment are radiation therapy, radiotherapy, irradiation, or x-ray therapy. Radiation works by making small breaks in the DNA inside cells. These breaks keep cancer cells from growing and dividing and cause them to die. Unlike chemotherapy, which usually exposes the whole body to cancer-fighting drugs, radiation therapy is usually a local treatment. In most cases, it's aimed at and affects only the part of the body being treated. Radiation treatment is planned to damage cancer cells, with as little harm as possible to nearby healthy cells. More than half of people with cancer get radiation therapy. Sometimes, radiation therapy is the only cancer treatment needed.

Apart from all these therapy I have given a detailed explanation of radiation therapy because in radiation therapy we use LINAC machine which is mainly used in Fricke gel dosimetry. External radiation (or external beam radiation): uses a machine that directs high-energy rays from outside the body into the tumor. Most people get external radiation therapy over many weeks. It's done during outpatient visits to a hospital or treatment center [13,14].

A linear accelerator (LINAC) customizes high energy x-rays or electrons to conform to a tumor 's shape and destroy cancer cells while sparing surrounding normal tissue. It features several built-in safety measures to ensure that it will not deliver a higher dose than prescribed and is routinely checked by a medical physicist to ensure it is working properly.

If the person scheduled for radiation therapy using a LINAC, the radiation oncologist will collaborate with a radiation dosimetrist and a medical physicist to develop a treatment plan for the patient. And doctor will double-check this plan before treatment begins and implement quality assurance procedures to ensure that each treatment is delivered in the exact same manner. A linear accelerator (LINAC) is the device most commonly used for external beam radiation treatments for patients with cancer. The linear accelerator is used to treat all parts/organs of the body. It delivers high-energy x-rays or electrons to the region of the patient's 29 tumor. These treatments can be designed in such a way that they destroy the cancer cells while sparing the surrounding normal tissue.

II. GEL DOSIMETRY SYSTEMS

Gel dosimetry systems are the only true 3-D dosimeters suitable for relative dose measurements. The dosimeter is at the same time a phantom that can measure absorbed dose distribution in a full 3-D geometry. Gels are nearly tissue equivalent and can be moulded to any desired shape or form.

Gel dosimetry can be divided into two types:

- Fricke gels based on the well established Fricke dosimetry;
- Polymer gels.

In Fricke gels, Fe^{2+} ions in ferrous sulphate solutions are dispersed throughout gelatin, agarose or PVA matrix. Radiation induced changes are either due to direct absorption of radiation or via intermediate water free radicals. Upon radiation exposure, ferrous ions Fe^{2+} are converted into ferric ions Fe^{3+} with a corresponding change in paramagnetic properties that may be measured using nuclear magnetic resonance (NMR) relaxation rates or optical techniques. A 3-D image of the dose distribution is created. A major limitation of Fricke gel systems is the continual post-irradiation diffusion of ions, resulting in a blurred dose distribution.

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The most widely used chemical dosimetry standard is the Fricke dosimeter.

- The Fricke solution has the following composition: 1mM FeSO4 or Fe(NH4)2(SO4)2 + 0.8N H2SO4 air saturated + 1mM NaCl.
- Irradiation of a Fricke solution oxidizes ferrous ions Fe2+ into ferric ions Fe3+ the latter exhibit a strong absorption peak at ג= 304 nm, whereas ferrous ions do not show any absorption at this wavelength.
- Radiation induced ferric ion concentration can be determined using spectrophotometry, which measures the absorbance (in OD units) of the solution.
- The response of the Fricke solution is determined first using the total absorption of an electron beam.

III. DOSIMETRIC BASIS FOR FRICKE GELS:

The dosimetric basis of the Fricke solution (an acidic oxygenated aqueous solution of ferrous ion, Fe2+) has been well established for decades: it is provided by the dose dependent transformation of ferrous (Fe2+) ions into ferric (Fe3+) ions. When the solution is irradiated, water decomposition occurs and hydrogen atoms produced react with oxygen to produce the hydroperoxy radical:

$H\bullet + O2 \rightarrow HO2\bullet$

Various reactions subsequently lead to the conversion of ferrous to ferric ions:

$Fe2+ + OH\bullet \rightarrow Fe3+ + OH-$
$Fe2+ + HO2\bullet \rightarrow Fe3++ HO2$
$HO2- + H3O+ \rightarrow H2O2 + H2O$, and
$Fe2++ H2O2 \rightarrow Fe3+ + OH\bullet + OH-$

The quantity of Fe3+ produced depends on the energy absorbed by the solution. Specifically, the change in ferric ion concentration is related to the radiation dose (energy per unit mass).

IV. MATERIALS AND METHODS:

A. FRICKE GEL PREPARATION:

❖ *Preparation Method for the Fricke Gel Dosimetry:*

➢ *Preparation of Stock Solution:*
1. Take 98 g of sulfuric acid (SA) and dissolved in 1 L de ionized water for preparing 1mole of stock solution
2. To prepare 50 mille mole of stock solution, take 50 ml of 1 mole sulfuric acid stock solution (which was prepared in the above point) and dilute it by adding 950 mille of water so now 1L of 50mille mole of stock solution ready.

➢ *XO-Stock Solution:*
1. Take 150 gm of 50milli mole of sulfuric acid stock solution
2. Measure Xo 0.11gm of and put in to 150 gm of sulfuric acid stock solution
3. Now 150 gm of 50millie mole of sulfuric acid stock solution with Xo ready (Xo stock solution).

➢ *FAS-Stock Preparation:*
1. Take 50 gm of 50millie mole of sulfuric acid stock solution.
2. Measure 0.12 gm of FAS and put into sulfuric acid stock solution.
3. Now 50gm of FAS Stock ready.
Additionally take 45 gm of 1mole sulfuric acid stock solution, 55gm of distilled Water, 40 gm of gelatin and 760 gm of distilled water.

➢ *Procedure:*
1. Take a cleaned beaker (2l). Fill up with 760 g of de ionized water.
2. Slowly pour 40 gm of gelatin.
3. Leave it for 20 minutes (at room. tem).
4. Now shift the beaker on stirrer set the temperature for 45 degree Celsius.
5. Now start to stirring after getting the clear solution cooled down the solution up to 32 degree Celsius.
6. Once reach 32 degree Celsius add 1 mole of sulfuric stock solution (45 gm).
7. Add 50 gm of Xo stock solution, 50 gm of FAS stock solution finally add 55 gm of pure distilled water.
8. Continually stirring the solution, after it comes cooled stage
9. Stop the stirring, Fricke solution displace in the container keep it for 4 degree Celsius for gellation.
10. The gel was put into 10×10×45 mm3 spectrophotometry cuvettes with two parallel optical faces 1 cm apart. The cuvettes with the gel were covered with caps and placed into a refrigerator for about 24 h in order to obtain transparent gel samples suitable for Spectrophotometric measurements.
11. The cuvettes with the gel were irradiated in the phantoms, and their absorbances were measured with a double-beam SPECORD® spectrophotometer (Analytik Jena AG, Germany) at λmax =585 nm.
12. The light beam of the spectrophotometer penetrates cuvettes in the central part of their lower halves, roughly 1.5 cm from the bottoms of the cuvettes.
13. In the irradiations with the linac, the cuvettes were positioned at the points of interest accordingly.

B. SYNTHESIS OF GOLD NANOPARTICLE

Citrate-stabilized gold nanoparticles were synthesized for this project. Chemicals and glassware needed are, gold chloride, DI water, sodium citrate, glass beaker, stir bar, strirrer/hotplate.

Step-by-step method for the synthesis of citrate stabilized gold nanoparticles (AuNPs) is as follows:

- In a glass beaker, add 250 l HAuCl4 (1% solution) to 18 mL DI water.
- Heat this solution until it starts to boil.
- Add 1 mL (0.5%) sodium citrate to this boiling solution.
- Continue the heating process until various color changes are observed. Color changes from clear to pale yellow to dark violet to deep purple to finally wine red.

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The obtained AuNPs are stored in dark under further use.

C. Fricke with AUNPs

➢ *For MV Radiation*

1. 3.5 ml of FXO was added into a cuvette and then 0.5ml of AUNPs were added.
2. And then the above prepared sample were irradiated for the following dose:- 0, 1, 2, 3, 4, 5 Gray.

➢ *For KV Radiation*

1. 3.5 ml of FXO was added into a cuvette and then 0.5ml of AUNPs were added.
2. And then the above prepared sample were irradiated for the following dose:- 0, 50, 75, 100, 150 Gray.

➢ *For 75 KV Radiation*

1. 3.0 ml of FXO was added into a cuvette and then the concentration of AUNPs were added in the following sequence:- 100, 200, 500, 1000 ul.
2. And then the above prepared sample were irradiated for the following dose:- 0, 1, 2, 3, 4, 5 Gray.

V. RESULTS AND DISCUSSION:

Fricke gel dosimetry of XO infused Fricke gel using gold nano particles.

The XO infused Fricke gel was irradiated to 6MV of energy using linear accelerator at a SSD of 75cm and field size of 10*10 and gel cuvette was irradiated to different doses from 0 to 6gy.

The dose response curve was seen using spectrophotometry, from the graph obtained using spectrophotometry shows the gel response and colour variation in different doses.

The XO infused Fricke gel was again irradiated to different KV of energies with same SSD of 75cm the range of energies are 50kv, 75kv and 100kv the gel response was seen mainly in 75kv.

Based on the graph obtained in 6MV of energy graph obtained and colour change in the cuvettes. 4gy of dose was taken as a constant dose for the next experiment, gold nano particles were added to the cuvettes of different concentration the enhancement of gold was seen.

Based on the graph obtained in 75kv as a constant dose the different concentration gold nano particle was added in the cuvettes and irradiated we could see the dose enhancement in the graph.

The aim of this work was to study the effect of AuNPs on enhancing the external beam radiation and monitor this change using XO infused Fricke Gel dosimetry.

The gel sample was subjected to same exposure time and distance but irradiation with energy field and doses was carried out.

The colour change in XO infused Fricke as seen visibly and through spectrophotometer was used to understand the effect of radiation and enhancement of this radiation effect to the presence of AuNPs.

In the first experiment, XO infused Fricke gel the XO infused Fricke gel was irradiated to 6MV of energy using linear accelerator at a SSD of 75cm and field size of 10*10 and gel filled cuvettes were irradiated to different doses from 0 to 4 Gy. The LINAC is capable for generating 6, 9, 12 and 15 MV radiations but only 6MV was chosen for this study. For this particular radiation, different dose – 1, 2 3 and 4 Gy was irradiated to the XO infused Fricke gel samples. The UV-vis absorption of the sample after exposure to the various radiations is shown in Figure 1. As you can see from the figure, as the dose increases, the peak intensity also increases in a linear fashion indicating a direct influence on radiation on Fricke gel. At the highest dose of 4Gy, there is a pronounced increase in the peak intensity.

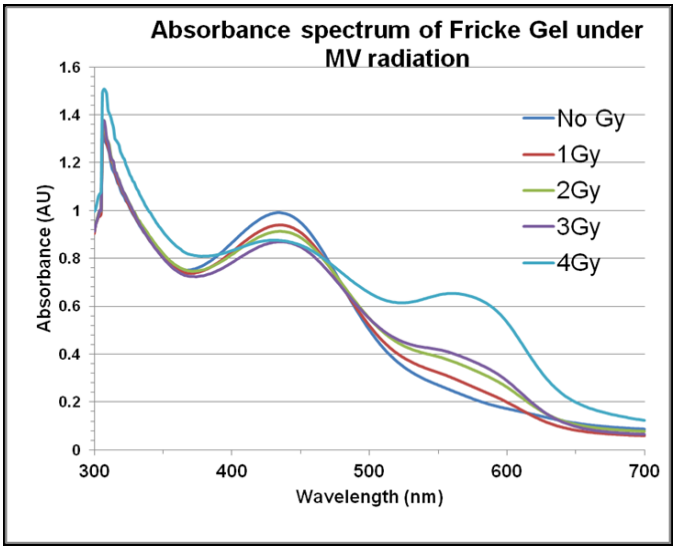

Fig 1:- UV-vis absorption spectrum of Fricke gel under MV radiation

Figure 2 is the absorption of XO infused Fricke gel irradiated using the same experimental condition but the sample now includes 500 □l of AuNPs. Similar to the observations in Figure 1, there is a linear dependency on radiation effect with increased radiation dose.

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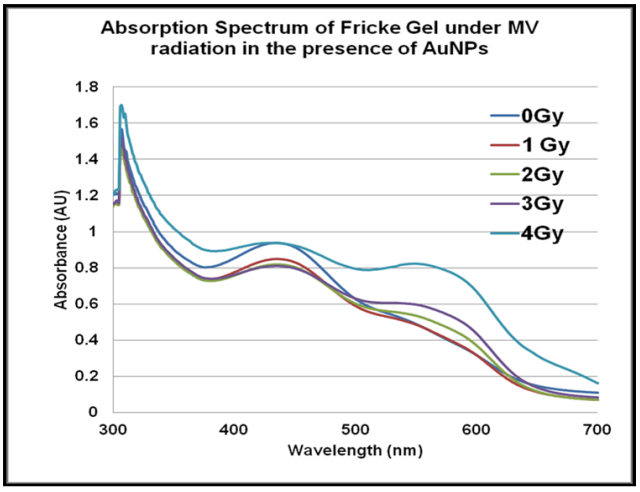

Fig 2:- UV-vis absorption spectrum of Fricke gel under MV radiation in the presence of AuNPs.

In order the study the actual effect of AuNPs in enhancing the given radiation dose, comparison was made of the absorption spectrum of XO infused Fricke gel exposed to 6MV, 4 Gy with and without AuNPs.

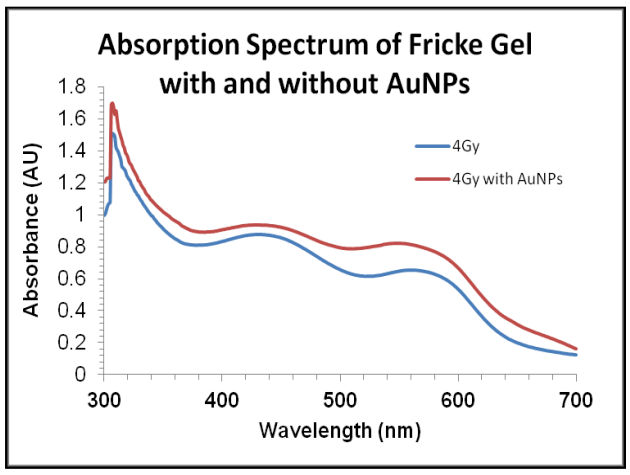

Fig 3:- Comparison of UV-vis absorption spectrum of XO infused Fricke gel exposed to 6MV radiation, 4 Gy, with and without AuNPs.

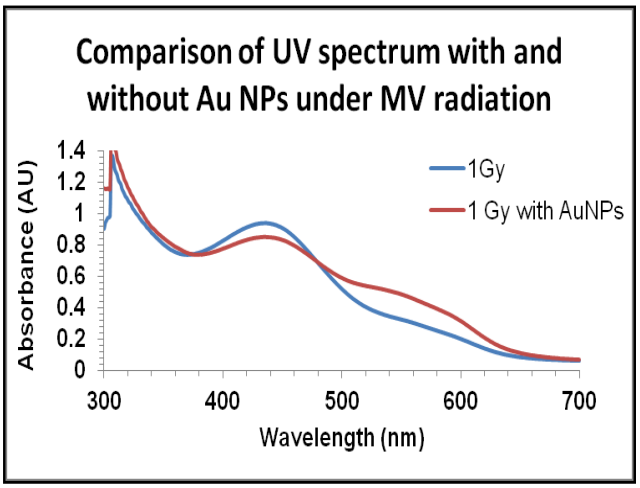

Fig 4:- Comparison of UV-vis absorption spectrum of XO infused Fricke gel exposed to 6MV radiation, 1 Gy, with and without AuNPs.

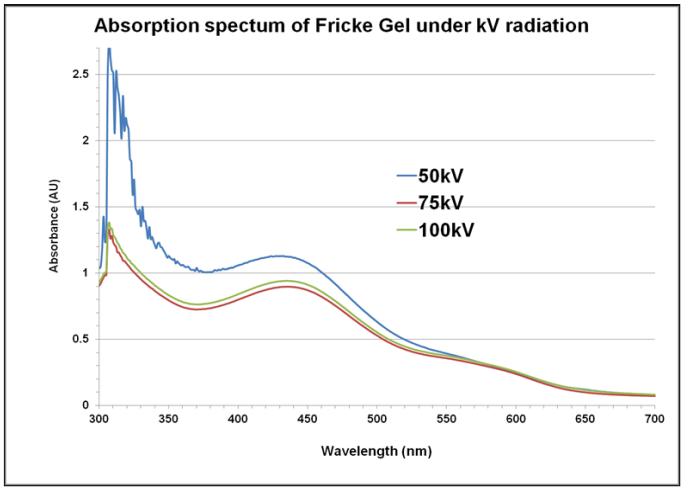

Fig 5:- UV-vis absorption spectrum of Fricke gel under kV radiation

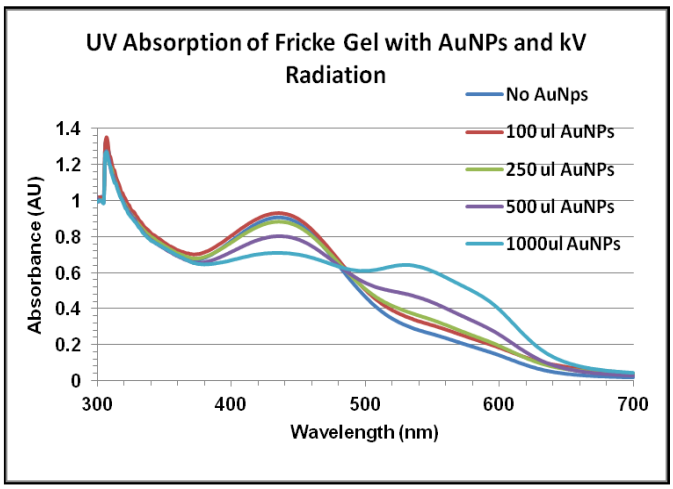

Fig 6: UV-vis absorption spectrum of Fricke gel under 75 kV radiation in the presence of different concentration of AuNPs.

The outcome of Fricke gel dosimetry can further be enhanced by the addition of certain additives. One such additive that has found a lot of application is the use of Xylenol orange (XO) that forms a stable colored complex with Fe2+ and Fe3+ ions in the visible region. XO is a chelating group and when complexed with ferrous and ferric salts, it forms two different types of color depending on its coordination. The representative illustration is shown in Figure 7. The complex that is formed has two distinct peaks (475 nm and 585 nm) in the visible region that can be qualitatively and quantitatively measured using UV-vis absorption spectrophotometer.

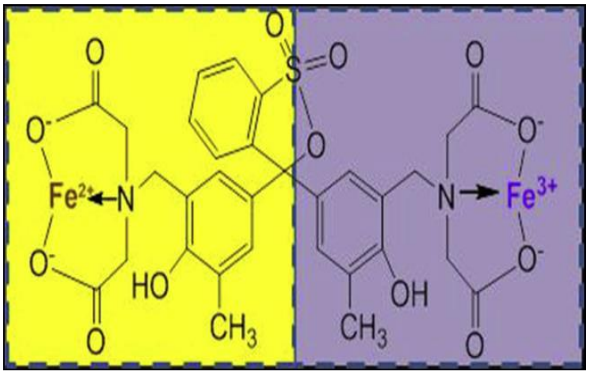

Fig 7:- Schematic illustration of complex formation between Xylenol Orange and ferrous and ferric ions

VI. CONCLUSIONS

The use of AuNPs for enhancement of radiation therapy has first been studies using Monte Carlo simulations and followed by in vitro and in vivo studies. It has been proven that presence of high-Z materials in the form nanoparticles can lead to radiation enhancement resulting in increased localization of the applied dose without harming the neigh boring healthy cells and tissue.

In this work, we have demonstrated the role of AuNPs in enhancing the radiation dose applied using the XO infused Fricke gel dosimetry. This method of dosimetry is an elegant and simple method that can be used to estimate the dose received in the area of interest. Using the UV-vis absorption spectroscopy as the tool, the effect of AuNPs in enhancing the dose both with high energy and low energy radiation has been demonstrated. The results indicate that presence of AuNPs in the vicinity of the tumor can have a very profound impact on the radiation therapy. In the future, the role of AuNPs will be further studied to improve its role in cancer nanotechnology and in radiation therapy.

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