DISCUSSION

Since its discovery, medical radiology has been one of the most popular applications of X-rays. In most cases, the contrast in radiology images is based on the different X-ray absorption of the different parts of a specimen. However, absorption is actually limited for X-rays. Weak absorption means small absorption differences among the tested materials, resulting in limited contrast thus low image quality. (137)

Contrast agents are used in radiographic imaging to provide additional information about vascular anatomy, to depict vascular flow and more recently, to determine the degree of perfusion. The most commonly used contrast materials are iodinated blood pool agents and physiologic information is limited to the vascular system and its extension into major organs. (138)

Nanotechnology is the understanding and control of matter generally in the 1 -100 nm dimension range. The application of nanotechnology concerns the use of precisely engineered materials at this length scale to develop novel therapeutic and diagnostic modalities. (139)

Nanomaterial's have unique physicochemical properties, such as ultra-small size, large surface area to mass ratio, and high reactivity, which are different from bulk materials of the same composition .These properties can be used to overcome some of the limitations found in traditional therapeutic and diagnostic agents. (140)

Nanoparticles agents continue to receive considerable attention in medical imaging for their potential as contrast agents. (141) Offering the advantages of greater biocompatibility and reduce toxicity compared to more conventional medical agents. (142)

Today a variety of nanoparticles systems are being investigated to explore their potential in molecular imaging, with many applications aimed at diagnosis or treatment cancer (143)

this study were built in two complementary pathways the first one was dealing with the radiological appearance of conventional contrast media (ultravest), nanoparticles and this was applied by constructing a set of phantoms and fill it with the appropriate nanoparticles then imaging it with different radiological modalities and the hounsfield unit (HU) were measured for each of them, the second pathway was to simulate the distribution of these nanoparticles on the constructed phantom and to measure the electric field presented on a specific nano materials which was the metal gold nanoparticles at five different concentrations which proved that contrast agent GNPs can be used for the noninvasive, in vivo detection of X-ray diagnoses with high resolution and specificity , since the electric field intensity has a greater value on gap distance between GNPs and on its edges w.r.t the electric field intensity on other areas.

A phantom in the setting of radiology research may be defined as animation or representation of an organ, body part, physiologic process or pathologic condition. Investigations employing phantoms are commonly performed in radiology research. (144)

In some instances a phantom study may serve as a pilot study prior to an investigation in living persons. Various types of phantoms may be used including phantoms made up of cadaveric, plastic, metallic and other materials. Our definition of a phantom also could include simulations obtained in living animals, as well as simulations obtained by digital image manipulation. [145]

In this study a set of different constructed phantoms were used:

Phantom 1: To verify the ability of the nanoparticles (GNPs, Fe_3O_4NPs, Cobalt NPs, nickel and titanium) and conventional contrast media (ultravest) as an X-ray contrast agent which are made up of a Plexiglas rectangle with dimensions 14 X 18 cm and 1cm height. Different cylindrical wells had been made in this phantom with dimensions 1 cm height and 1 cm radius. (5 - 6 holes for each nanomaterial),

Phantom 2: To verify the ability of the nanoparticles (GNPs, Fe_3O_4NPs) as an X-ray contrast agent, we constructed a phantom made of a plastic tubes which are represented as blood vessels and it is constructed from a plastic tubes with length 30 cm and diameter 3mm where filled with blood an then injected with gold and iron oxide nanoparticles during imaging using CT and conventional x-ray.

Phantom3: To verify the ability of the nanoparticles as a conventional x-ray, CT and MRI a 1 ml of the different nanoparticles used (Gold, Fe_3O_4, Cobalt, Nickel and Titanium) with different concentrations was mixed with 1ml of human blood and injected in aplastic tube with 1cm diameter and 5cm height.

Phantom4: To verify the ability of the nanoparticles as an CT and MRI a 1 ml of nickel and titanium nanoparticles with different concentrations was mixed with 1 ml gel material in a plastic tube with 1cm diameter and 5cm height,

Phantom 5: To verify the ability of the nanoparticles as an Ultrasound contrast agent, it had been made up of a plastic container which is filled with 350 ml of gel material and the test tube which containing the nanoparticles were placed at the bottom of this container then imaged using linear ultrasound probe with power 7.5 MHZ in Longitudinal and transverse positions.

Leon Smith et al. [146] proved that nanoparticles offer enormous potential for improving cancer imaging and treatment. With demonstrated success in existing diagnostic imaging.

Hainfeld J F et al [147] reported that current contrast agents impose serious limitations on medical imaging, short imaging times, the need for catheterization in many cases, occasional renal toxicity and poor contrast in large patients. They demonstrated that gold nanoparticles may overcome these limitations. Gold has higher absorption than iodine with less bone and tissue interference achieving better contrast with lower x-ray dose. Nanoparticles clear the blood more slowly than iodine agents, permitting longer imaging times.

Guojia H et al [148] successfully tested the feasibility of antibiofouling polymer coated gold nanoparticles as duel model contrast agent for x-ray and photoacoustic imaging they demonstrated that the nanoparticles have high intensity due to elevated optical absorption

the combined imaging method are complementary and together they provide the rich information needed for reliable detection and diagnosis.

Present nanoparticles that are under development include gold nanoparticles for X‑ray contrast enhancement, magnetic nanoparticles for magnetic resonance imaging (MRI) enhancement. And even hybrid nanoparticles containing iron oxide and gold in a polymer coating, serve contrast agents for both computed tomography (CT) and MRI. [138-148] In this study we had studied other several nanoparticles as contrast agents which include cobalt NPs, titanium NPs a nickel NPs with different concentrations which offer a particular advantage in different degrees as a contrast agent for MRI specially nickel NPs.

Sungsook Ahn et al [149] proved that: Au NPs can offer a particular advantage as a tracer and a contrast enhancer in X-ray imaging technologies by sensing the variation in X-ray attenuation in a given sample volume. In this study we agreed that Au nanoparticles had proved an advantage as a contrast agent in x-ray imaging.

Avnika T and Garima G, [150] Gold nanoparticles have advantages over other metal nanoparticles due to their biocompatibility and non-cytotoxicity. Evan Boote et al, [138] CT imaging of the phantom showed that for very low concentrations, on the order of several hundred micrograms of Au per gram of background material (agarose), the high Z and density of the Au NPs was able to produce a change in the x-ray attenuation sufficient to change the HU value.

In this study The HU measurement of CT images for Gold, iron oxide and cobalt nanoparticles diluted in water and blood in phantom one, two and three improved that the Au NPs with different concentrations (0.1, 0.05, 0.025, 0.0125 and 0.00625 mg/ml) has a higher (HU) value than Fe_3O_4 and Co NPs and Fe_3O_4 is higher than Co NPs the HU measurement decreases with decreasing the NPs concentration, and the measured MRI signal intensity for gold, iron oxide and cobalt nanoparticles with different concentration improved that GNPs has higher signal intensity than Co NPs and Fe_3O_4 and Co NPs is higher than Fe_3O_4 also the measurement decreases with decreasing the NPs concentration.

Leon Smith et al. [146] proved that Titanium dioxide nanoparticles as potential dual-mode imaging and therapy enhancement agents indicate they are a promising candidate for image contrast in computed tomography. In our study the HU measurement of CT images for titanium NPs compared with Nickel nanoparticles diluted in blood in phantom three improved that the titanium NPs has a higher attenuation (HU) value than Nickel NPs, while in the signal intensity measurement of MRI images for Nickel and titanium nanoparticles diluted in blood in phantom four improved that the Nickel NPs has a higher value than titanium NPs.

Jun Liu et al. [251] reported that the feasibility of using targeted nanoparticles to enhance ultrasonic images was demonstrated in vitro. This may be a promising approach to target cancer biomarkers for site-specific ultrasound imaging.

The Ultrasound images performed for the test tube containing the GNPs proved that there is a different in echogenicity between different concentrations of the nanoparticles but it was not significant seen by the true eye in the transverse images (which appears as a hyper echoic circular object) but little significant in the longitudinal images (which appears

as a longitudinal tube with different echogenicity)and shows that the degree of echogenicity decreases with decreasing concentration of the nanoparticles.

Ultrasound images performed for the test tube containing the Fe_3O_4 nanoparticles proved that there is a significant difference seen by the true eye in the transverse and longitudinal images and shows that the degree of echogenicity decreases with decreasing concentration of the nanoparticles. which we consider it as a promising approach to target cancer biomarkers for site-specific ultrasound imaging.

Lasagna-Reeves et al [152] tested if GNPs treatment produces sub-acute toxicity in mice during the course of the study. They observed no mortality or any gross behavioral changes in mice receiving GNPs. no evidence of atrophy, congestion, or inflammation were observed. To further search for abnormalities, the weight coefficient of each organ to body was calculated. No significant differences were observed for any of the organs studied as compared with controls untreated animals. to determine if GNPs produce renal toxicity they determined the levels of urea nitrogen, creatinine total bilirubin and alkaline phosphatase in blood and hepatic and biliary functionality in addition determining the levels of uric acid since hypouricemia (decrease of uric acid in the blood) is a common sign of drug toxicity. and as these parameters compared to controls showed no statically significant differences in any of the parameters tested.

The modeling and simulation was performed in CST STUDIO SUITE electromagnetic simulation software. Preliminary simulation and proof of concept were conducted in CST STUDIO Designer, while the complete simulation was conducted in CST STUDIO frequency domain solve.

In computational study of the EF intensity distribution around nanoparticles in phantom I: The Gap Distance between GNPs was determined between two neighboring GNPs, in different concentrations, since the radios of a single GNPs which is (2.5 nm), so the volume of it can be determined, by multiply volume of a single GNPs by the density of each sample we get the mass of a single GNPs , by dividing the total mass by the mass of a single GNPs we get the total number of GNPs in each concentration in cm3

The following calculations were used to determine the gap distance between GNPs for different concentration: After calculating the total number of GNPs in each concentration in cm3, Taking the cubic root we get the number of GNPs in a one cm3, Taking the inverse of the number of GNPs in a one cm we get the space between GNPs in cm units, Multiplying this space by 107, we get the space between GNPs in nm units.

The represented EF intensity distribution on the gap distance between GNPs and on the inner and outer edges of them for the five concentrations of GNPs results includes: By decreasing the concentrations the gap distances (S) increases gradually from (23 nm) at concentration (1) , until it reach (59 nm) at concentration (5), The multipacks electric field at the gap distance decreases gradually from (1.0475V/m) at concentration (1), until it reach (0.9660 V/m) at concentration (5), The EF at the inner edges of GNPs fluctuated during the five concentrations between (1.0885 V/m) and (1.1528V/m), The EF at the outer edges of GNPs fluctuated during the five concentrations between (1.2960 V/m) and (1.1372V/m), The average of EF intensity of all EF value (midpoint , outer edges of GNPs 1, inner edges of GNPs 1, outer edges of GNPs 2,and inner edges of GNPs 2) have value ≈ 1 V/m.

In computational Study of EF distribution around nanoparticles in phantom II: The description of 2D of the Electric field (EF) intensity distribution for GNPs for different concentrations is applicable for the near-field region, in which the quasi-static approximation is valid. However, when the inter-particle distance is increased to the order of the wavelength, diffractive contributions start playing an important role. Zou et al. [130] studied a one-dimensional array of nanoparticles, of various sizes with various spacings. They found that the scattered light showed the features of the individual dipoles, as well as diffractive features of the entire array.

In computational study of the attachment of NPs on cancer cell: The Gold nanostructures optical skills, which depend on the size, shape, and dielectric constant of nanoparticles, enable applications where particles are used as imaging and sensing probes.

The GNPs are injected through the blood circulatory system which delivered them to the site of the targeting cancer, and since GNP is 100 smaller than the red blood cell its own the unique ability of passing through tissue molecules and would only seek out cancer cells, leaving healthy cells and tissue untouched, then it will attach to the surface membrane of the cancer cell.

Cancer cells are generally larger than normal cells and its dimension in the range of micrometer (μm), for demonstration, simulate the imaging of a sphere cancer cell of a diameter (TD=1 μm) surrounded by an array of GNPs consisting of 36 GNP each of a diameter (PD=100 nm)

The cancer targeted agent, NGP can be used for the noninvasive, in vivo detection of cancerous cells with high resolution and specificity. In the future, this agent may be improved by development of small peptide-based ligands and through the possible attachment to nanoparticles for delivery of imaging contrast and therapy. Also it could be used for hyperthermia cancer treatment.