WO 2011/127061 A1 relates to a method for enhancing the effect of radiation directed to a tissue or a population of cells comprising the steps of: (1) administering to an animal an amount of high-Z particles, the high-Z particles comprising a targeting molecule with an affinity for a targeted tissue or a targeted population of cells and a high-Z element; and (2) subsequently irradiating the targeted tissue or targeted population of cells with ionizing radiations; wherein the high-Z particles are administered to the animal in an amount sufficient to achieve a concentration in the targeted tissue or targeted population of cells of less than 0.05% metal by weight.

Inventors herein provide a new and powerful strategy to use their nanoparticles (herein below described) which are able to achieve a very efficient alteration or destruction of target cancerous cells in combination with ionizing radiations, when said nanoparticles are adequately selected and concentrated inside the targeted cancer site, as herein demonstrated.

SUMMARY OF THE INVENTION

In one aspect, there is provided a composition inducing in a human subject having a tumor (i) the destruction of more than 30% of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction when the volume (Vc) of said composition occupies between 2 and 50% of the tumor volume (Vt) and when the tumor is exposed to ionzing radiations, wherein the composition comprises inorganic nanoparticles having a volume (Vin) having an electron density at least 5 times the electron density of the corresponding volume 1 (Vw1) of water.

In another aspect, there is provided a use of a composition described herein in the manufacture of a medicament for (i) the destruction of more than 30% of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction when the volume (Vc) of said composition occupies between 2 and 50% of the tumor volume (Vt) and when the tumor is exposed to ionizing radiations, in a human subject having a tumor.

~~Inventors now~~In another embodiment, there is provided an advantageous composition comprising inorganic particles for use for treating cancer, in particular a composition allowing the destruction of more than about 30%, preferably more than about 44% or more than about 47%, even more preferably more than about 70%, of cancer cells in a tumor volume of a subject (histological response assessment) or inducing at least more than 20% of tumor size reduction (anatomical response assessment) in a subject or inducing at least more than 20% of tumor ^{18}F-FDG SUV (Standardized Uptake Value) decline (metabolic response assessment) in a subject, when the tumor of said subject is exposed to ionizing radiations.

Once administered, the volume (Vc) of the composition of the invention occupies between 2 and 50% of the tumor volume (Vt). Each inorganic nanoparticle of the composition has a volume (Vin) having an electron density at least 5 times the electron density of the corresponding volume 1 (Vw1) of water.

In a particular embodiment, a method for inducing in a subject suffering of a cancer (i) the destruction of more than 30% of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction is herein described. This method comprises:

- administering in a subject suffering of a cancer a composition comprising inorganic nanoparticles, each of said inorganic nanoparticle having a volume (Vin) having an electron density at least 5 times the electron density of the corresponding volume 1 (Vw1) of water, and
- exposing the tumor (targeted tissue or targeted population of cells) of the subject to ionizing radiations,

thereby inducing (i) the destruction of more than 30% of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction when the volume (Vc) of said composition occupies between 2 and 50% of the tumor volume (Vt).

The present document further describes the use of inorganic nanoparticles to prepare a composition for inducing in a subject suffering of a cancer (i) the destruction (pathological response) of more than about 30%, preferably more than about 44% or 47%, even more preferably more than about 70%, of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction (tumor shrinkage), when the volume (Vc) of said composition occupies between 2 and 50% of the tumor volume (Vt) and when the tumor is exposed to ionizing radiations, wherein each inorganic nanoparticle has a volume (Vin) having an electron density at least 5 times the electron density of the corresponding volume 1 (Vw1) of water.

In a preferred embodiment, said volume composition (Vc) has an electron density of at least 3% of the electron density of the corresponding volume 2 (Vw2) of water, and even more preferably said inorganic nanoparticles provide more than $3x10^{22}$ electrons, preferably more than $7x10^{22}$ electrons, to the tumor mass.

In a further preferred embodiment, these inorganic nanoparticles provide more than $3x10^{22}$ electrons, preferably more than $7x10^{22}$ electrons to the tumor mass. In another preferred embodiment, the volume composition (Vc) (advantageously further) has an electron density of at least 3% of the electron density of the corresponding volume 2 (Vw2) of water (Figure 1).

Results presented for the first time in the context of the present ~~invention~~ disclosure now demonstrate that a composition comprising high electron density inorganic nanoparticles occupying between 2 and 50% of the tumor volume are able to induce at least more than about 30%, preferably more than about 44% or 47%, even more preferably more than about 70% of cancer cell killing when the inorganic nanoparticles provide at least, preferably more than $3x10^{22}$ electrons, for example more than about $3.2x10^{22}$ electrons, preferably more than $7x10^{22}$, electrons to the tumor mass. Each nanoparticle of the composition advantageously has an electron density at least 5 times the electron density of the same nanoparticle composed of water molecules.

DETAILED DESCRIPTION OF THE INVENTION

INORGANIC NANOPARTICLE

SIZE

In the spirit of the invention, the term "**nanoparticle**" refers to a product, in particular a synthetic product, with a size in the nanometer range, typically between 1 nm and 500 nm.

10. Composition according to anyone of claims 1 to 9, wherein inorganic nanoparticles are administered to the subject through a route selected from the intratumoral, the intraarterial or the intravenous route.

11. Composition according to anyone of claims 1 to 10, wherein ionizing radiations sources are selected from X-rays, typically X-rays of between 50 KeV and 6 MeV, ion beams, electron beams, gamma-rays, a radioactive isotope.

12. Use of a composition according to any one of claims 1-11 in the manufacture of a medicament for (i) the destruction of more than 30% of cancer cells in a tumor volume or (ii) at least more than 20% of tumor size reduction when the volume (Vc) of said composition occupies between 2 and 50% of the tumor volume (Vt) and when the tumor is exposed to ionizing radiations, in a human subject having a tumor.