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# Causes of Cancer in Patients and its Treatment

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## **Abstract**

The current scenario for cancer research is wide, offering many possibilities for the constant improvement of treatment, considering not only patient recovery but also caring for their well-being during therapy.

**Keywords:** Well-being; Cancer medicine; Increment of temperature; Nanoparticles; Theranostic; Imaging purposes

# Introduction

However, some disadvantages still have to be overcome to improve their performances. Much progress has been made, but many others are likely to come in the near future, producing more and more ad hoc personalised therapies. Nanoparticles are small systems with peculiar physicochemical properties due to their size and high surface-tovolume ratio. Biocompatible nanoparticles are used in cancer medicine to overcome some of the issues related to conventional therapies, such as the low specificity and bioavailability of drugs or contrast agents. Therefore, encapsulation of the active agents in nanoparticles will increase their solubility/biocompatibility, their stability in bodily fluids and retention time in the tumour vasculature. Furthermore, nanoparticles can be engineered to be extremely selective for a precise target and to release the drug in a controlled way by responding to a specific stimulus [1]. This is the case of ThermoDox, a liposomal formulation that can release doxorubicin as a response to an increment of temperature. Inorganic nanoparticles are generally used as contrast agents for diagnosis purposes. Among them, quantum dots are small light-emitting semiconductor nano-crystals with peculiar electronic and optical properties, which make them highly fluorescent, resistant to photo bleaching and sensitive for detection and imaging purposes. Combined with active ingredients, they can be promising tools for theranostic applications [2]. In a recent study, quantum dots coated with polyethylene glycol were conjugated to anti-HER2 antibody and localised in specific tumour cells. Superparamagnetic iron oxide nanoparticles are usually exploited as contrast agents in magnetic resonance imaging because they interact with magnetic fields. Five types of SPIONs have been tested for MRI: ferumoxides, ferucarbotran C, ferumoxtran-10. Ferucar-botran is currently available in few countries, while the others have been removed from the market. SPIONs have also been studied for cancer treatment by magnetic hyperthermia, and a formulation of iron oxide coated with aminosilane called Nanotherm has been already approved for the treatment of glioblastoma. Gold nanoparticles have raised interest because of their optical and electrical properties and low toxicity. They are mainly used as contrast agents for X-ray imaging, computed tomography, photoacoustic imaging and photodynamic therapy [3].

# **Discussion**

A nanoshell made of a silica core and a gold shell coated with PEG was approved by the Food and Drug Administration in 2012 and commercialised as AuroShell for the treatment of breast cancer by photodynamic therapy. Organic nanoparticles are mainly used as delivery systems for drugs. Liposomes and micelles are both made of phospholipids, but they differ in their morphology [4]. Liposomes are spherical particles having at least one lipid bilayer, resembling the structure of cell membranes. They are mainly used to encapsulate hydrophilic drugs in their aqueous core, but hydrophobic drugs can

also be accommodated in the bilayer or chemically attached to the particles. The interaction with the current causes the oscillation of ions in the extracellular fluid, which, in turns, produces heat. The more conductive the medium, the more effective the process. For this reason, RF ablation works very well in the liver and in other areas with a high content of water and ions, whereas it has a poor effect in lungs. Moreover, the efficiency of the treatment decreases with the size of the lesion, giving the best results for areas not larger than 3 cm 2 Microwave ablation is based on the electromagnetic interaction between microwaves and the polar molecules in tissues, like water, that causes their oscillation and the consequent increase in temperature. Unlike the electrical current in RF ablation, microwaves can propagate through any kind of tissue, and this allows high temperatures to be reached in a short amount of time, to have a deeper penetration and to treat larger areas of tumours. Laser therapy exploits the properties of laser beams of being very narrow and extremely focused at a specific wavelength. This makes the treatment very powerful and precise, thus a promising alternative to conventional surgery. The absorption of the light emitted by the laser results in the heating and subsequent damage of the treated area. Depending on the specific application, different kinds of lasers can be used. Neodymium lasers and diode lasers are used to treat internal organs, since they have a penetration depth [5]. Conversely, CO 2 lasers, with a penetration depth are used for superficial treatments. Laser therapy is receiving a lot of attention in research because of its advantages compared to other ablation techniques, such as a higher efficacy, safety and precision, and a shorter treatment session needed to achieve the same results. Moreover, the fibres to transmit laser light are compatible with MRI, allowing for a precise measure of the temperature and the thermal dose. However, there are still some limitations to overcome, such as the need of a very skilled operator to place the fibre in the correct position. Finally, a new way to heat tumour tissues, currently under study, is through magnetic hyperthermia. This technique exploits super paramagnetic or ferromagnetic nanoparticles that can generate heat after stimulation with an alternating magnetic field. The most studied systems in nano-medicine are SPIONs. The production of heat, in this case, is due to the alignment of magnetic domains in the particles when the magnetic field is applied, and the

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subsequent relaxation processes during which heat is released, when the magnetic field is removed and the magnetisation of the particles reverts to zero. Magnetic hyperthermia can reach any area of the body and SPIONs can also act as MRI contrast agents to follow their correct localisation before the stimulation [6]. The particles can be coated with biocompatible polymers and/or lipid and functionalized with specific ligands to impart targeting properties. As already mentioned, until now, just a formulation of 15-nm iron oxide nanoparticles coated with aminosilane obtained approval for the treatment of glioblastoma. SPIONs have also been successfully encapsulated in lipid nano-carriers together with a chemotherapeutic agent to combine chemotherapy and hyperthermia. Efficient cancer therapy currently relies on surgery and, in approximately 50% of patients, on radiotherapy, which can be delivered by using an external beam source or by inserting locally a radioactive source, thus obtaining focused irradiation. Currently, localisation of the beam is facilitated by image-guided radiotherapy, where images of the patient are acquired during the treatment allowing the best amount of radiation to be set [7]. Thanks to the introduction of intensity-modulated radiotherapy, radiation fields of different intensities can be created, helping to reduce doses received by healthy tissues and thus limiting adverse side effects. Finally, by means of stereotactic ablative radiotherapy, it has become feasible to convey an ablative dose of radiation only to a small target volume, significantly reducing undesired toxicity. Unfortunately, radio-resistance can arise during treatment, lowering its efficacy. This has been linked to mitochondrial defects; thus, targeting specific functions have proven to be helpful in restoring anti-cancer effects. A recent study has shown, for example, that radio-resistance in an oesophageal adenocarcinoma model is linked to an abnormal structure and size of mitochondria, and the measurement of the energy metabolism in patients has allowed discrimination between treatment resistant and sensitive patients [8]. Targeting mitochondria with small molecules acting as radiosensitizers is being investigated for gastrointestinal cancer therapy. Cancer is a complex disease and its successful treatment requires huge efforts in order to merge the plethora of information acquired during diagnostic and therapeutic procedures. The ability to link the data collected from medical images and molecular investigations has allowed an overview to be obtained of the whole tri-dimensional volume of the tumour by non-invasive imaging techniques [9]. This matches with the main aim of precision medicine, which is to minimise therapy-related side effects, while optimising its efficacy to achieve the best individualised therapy. Radiomics and pathomics are two promising and innovative fields based on accumulating quantitative image features from radiology and pathology screenings as therapeutic and prognostic indicators of disease outcome. Many artificial intelligence technologies, such as machine learning application, have been introduced to manage and elaborate the massive amount of collected datasets and to accurately predict the treatment efficacy, the clinical outcome and the disease recurrence. Prediction of the treatment response can help in finding an ad hoc adaptation for the best prognosis and outcome. Nowadays, personalised medicine requires an integrated interpretation of the results obtained by multiple diagnostic approaches, and biomedical images are crucial to provide real-time monitoring of disease progression, being strictly correlated to cancer molecular characterisation. Radiomics is intended as the high throughput quantification of tumour properties obtained from the analysis of medical images. Pathomics, on the other side, relies on generation and characterisation of high-resolution tissue images. Many studies are focusing on the development of new techniques for image analysis in order to extrapolate information by quantification and disease characterisation. Flexible databases are required to manage big volumes

of data coming from gene expression, histology, 3D tissue reconstruction and metabolic features in order to identify disease phenotypes [10]. Currently, there is an urgent need to define univocal data acquisition guidelines. Some initiatives to establish standardised procedures and facilitate clinical translation have been already undertaken, such as quantitative imaging network or the German National Cohort Consortium. Precise description of the parameters required for image acquisition and for the creation and use of computational and statistical methods is necessary to set robust protocols for the generation of models in radiation therapy. According to the US National Library of Medicine, clinical trials involving radiomics are currently recruiting patients, and a few have already been completed. In recent years, research into cancer medicine has taken remarkable steps towards more effective, precise and less invasive cancer treatments. While nano-medicine, combined with targeted therapy, helped improving the bio-distribution of new or already tested chemotherapeutic agents around the specific tissue to be treated, other strategies, such as gene therapy, siRNAs delivery, immunotherapy and antioxidant molecules, offer new possibilities to cancer patients. On the other hand, thermal ablation and magnetic hyperthermia are promising alternatives to tumour resection.

# Conclusion

Finally, radiomics and pathomics approaches help the management of big data sets from cancer patients to improve prognosis and outcome. At the moment, the most frequent entries concerning cancer therapies in the database of clinical trials involve the terms targeted therapy, immunotherapy and gene therapy, highlighting that these are the most popular methodologies under investigation. In particular, radiomics, immunotherapy and exosomes are the entries whose number has increased the most in the last 10 years.

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## Conflict of Interest

None

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