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Cancer therapy: radiopharmaceuticals enable personalised medicine

(Vienna, 18 October 2012) Taking radioactive substances as drugs? At first sight, many would undoubtedly reject this idea. But radioactivity can indeed be a healing force. "As part of a precisely planned and individually tailored treatment, radiopharmaceuticals are a very efficient weapon in fighting various kinds of tumours," says Dr Glenn Flux, physics expert of the European Association of Nuclear Medicine (EANM).

"We are at the outset of a dramatic improvement in cancer therapy as we move towards individually tailored programmes using radiopharmaceuticals for both diagnosis as well as treatment. This allows accurately targeted tumour destruction while at the same time reducing harmful side effects to a minimum," says EANM expert physicist Dr Flux. This concept is applicable to various kinds of tumours ranging from thyroid cancer and neuroendocrine tumours to bone marrow metastases from prostate cancer and liver tumours. The basic concept of molecular radiotherapy is simple: radioactive molecules are attached to a substance that targets cancer cells. The radioactivity then serves two functions. As the activity decays, beta particles are emitted that due to their mass travel only a short distance within tissue, irradiating and destroying the cancer cells. Simultaneously, gamma rays are emitted that penetrate the patient and can then be captured by a specially designed scintillation camera which provides the doctor with a computer image of the distribution of the radionuclide within the patient. By this he can make sure that the cancer has been targeted to greater extent than any normal tissues.

Enormous potential

"The potential of this procedure for personalised treatment is enormous, but has not yet been fully utilised," says Dr Flux. According to him, it has been standard practice in molecular radiotherapy for decades to administer the same level of radioactivity in all patients, only sometimes modified by the patient's weight. "Recent research, however, shows that these levels can lead to widely varying absorbed doses, that is, amounts of radiation energy being deposited in the tissue. For example, in one study it was shown that absorbed doses delivered to thyroid tissues from a single administration of 3,000 MBq radioiodine varied from 7 Gy to 570 Gy in different patients," says Dr Flux. In contrast, all patients receiving more conventional external beam radiation treatment will receive the same dose for any given treatment.

Intensive research is now underway in order to transform the combination of radiopharmaceutical diagnosis and treatment into a personalised therapeutic approach and thus render it more precise. Increasingly sophisticated computer techniques allow doctors not only to control whether radioactivity was delivered to the desired target, but also to

measure the absolute level of this activity. Also, the absorbed doses can be established through increasingly accurate calculations performed on series of scans.

Much to gain from radiotherapy

How are cancer patients to benefit from these developments? Dr Flux gives an example: “It has been demonstrated that not only do different tumours and different patients take up different fractions of administered activity, but that this activity is washed out at different rates. A protocol designed to treat children with neuroblastoma with I-131 mIBG (Meta-iodobenzylguanidine, which is taken up by cells that produce adrenalin and therefore targets cancers of the sympathetic nervous system) according to their individual uptake has been developed over many years and is poised to be the subject of a European clinical trial in high-risk patients that fail initial chemotherapy. It has been shown that while the biokinetics of different patients vary widely, a second administration will follow the same pattern as the first in most patients so that if a treatment is given in two or more fractions, the activity can be modified as the treatment progresses. This ensures that all patients receive the same absorbed dose. In a pilot study this has already shown to predict the toxicity that will limit the treatment.”

But there is even more to gain from molecular radiotherapy as it may be used not just in isolation, but also in addition to external beam radiotherapy or to chemotherapy. Because the uptake mechanisms of cells for radiopharmaceuticals are often different to the targeting mechanism of chemotherapeutic drugs, the two may be given together. It has also been shown that some other drugs can enhance the effect of radiation. “These are promising new paths indicating that radiopharmaceuticals are going to be key in our fight against cancer,” says Dr Flux.

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