TARGETED RADIONUCLIDE THERAPY - PRACTICE OF TARGETING CONFIRMATIVE THERAPY, AN INDIVIDUALIZED IMAGE-BASED TREATMENT

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In Japan, 4 types of targeted radionuclide therapies (TRT) are currently available in routine use including \(^{131}\text{I-}\)sodium iodide for thyroid cancer and hyperthyroidism, \(^{131}\text{I-}\)metaiodobenzylguanidine (MIBG) for malignant neuroendocrine tumors such as pheochromocytoma and neuroblastoma, \(^{90}\text{Y-}\)labaled murine monoclonal IgG1 for B-cell lymphoma (radioimmunotherapy) (Zevalin\(^{\text{®}}\)), and \(^{89}\text{Sr-}\)strontium chloride (Metastron\(^{\text{®}}\)) for palliation of painful bone metastases. \(^{131}\text{I-}\) is taken up by cancer cells originating from thyroid follicular cells via Na/I symporters. \(^{131}\text{I-MIBG}\) is targeted to neuroendocrine tumor cells via active transport through the uptake-1 mechanism. Zevalin binds to CD20 cell surface antigens on lymphoma cells. \(^{89}\text{Sr}\) is an analog of calcium that accumulates in metastatic bone lesions. Because of these targeting mechanisms, TRT is a true form of molecular targeted therapies.

As many of radionuclides emit \(\gamma\) ray or positron, \textit{in vivo} distribution of radiopharmaceuticals can be delineated by scintigraphic technique with single photon computed tomography (SPECT) or positron emission tomography (PET), which makes TRT a surely unique therapeutic modality. That is, we can confirm targeting of radiopharmaceuticals in lesions. Furthermore, their distribution in normal tissues can be simultaneously monitored. In addition, we can obtain changes in their distribution with sequential image acquisition, which provides pharmacokinetic data on them. These features enable us predict therapeutic response of lesions and possible adverse reaction. Therefore, TRT is patient-specific, tailored treatment. Based on these concepts of TRT, we would like to propose to call TRT targeting confirmative therapy (TCT).

Therapeutic effects are currently provided with \(\beta\) particles of radionuclides. Cells within millimeter path length of \(\beta\) particles are irradiated, so that it is not necessary to target all cells in lesions. In addition, many of them are irradiated by several \(\beta\) rays (cross-fire effects), making the advantage of TRT over non-radioactive pharmaceuticals. Alfa emitters with high LET (linear energy transfer) and RBE (relative biological effectiveness) are candidates for the next generation of therapeutic radionuclides.

TRT can be achieved by a variety of molecules such as ionic forms of radionuclides and radiolabeled compounds of antibodies, peptides, synthetic amino acids, nucleotides, receptor ligands, and substrates for transporters, which compose of a broad range of sizes from atoms to nanoparticles. In developing novel radiopharmaceuticals, animal SPECT/PET combined with CT/MRI has been fully utilized. SPECT/PET possesses extremely high sensitivity of signal detection that enables delineation of molecular targeting at nano-molar range. Radiopharmaceutical developed at benches can be directly brought to bedsides. TRT is an individualized image-based treatment.

Biography

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