Present and Future of Theranostic Radioisotopes

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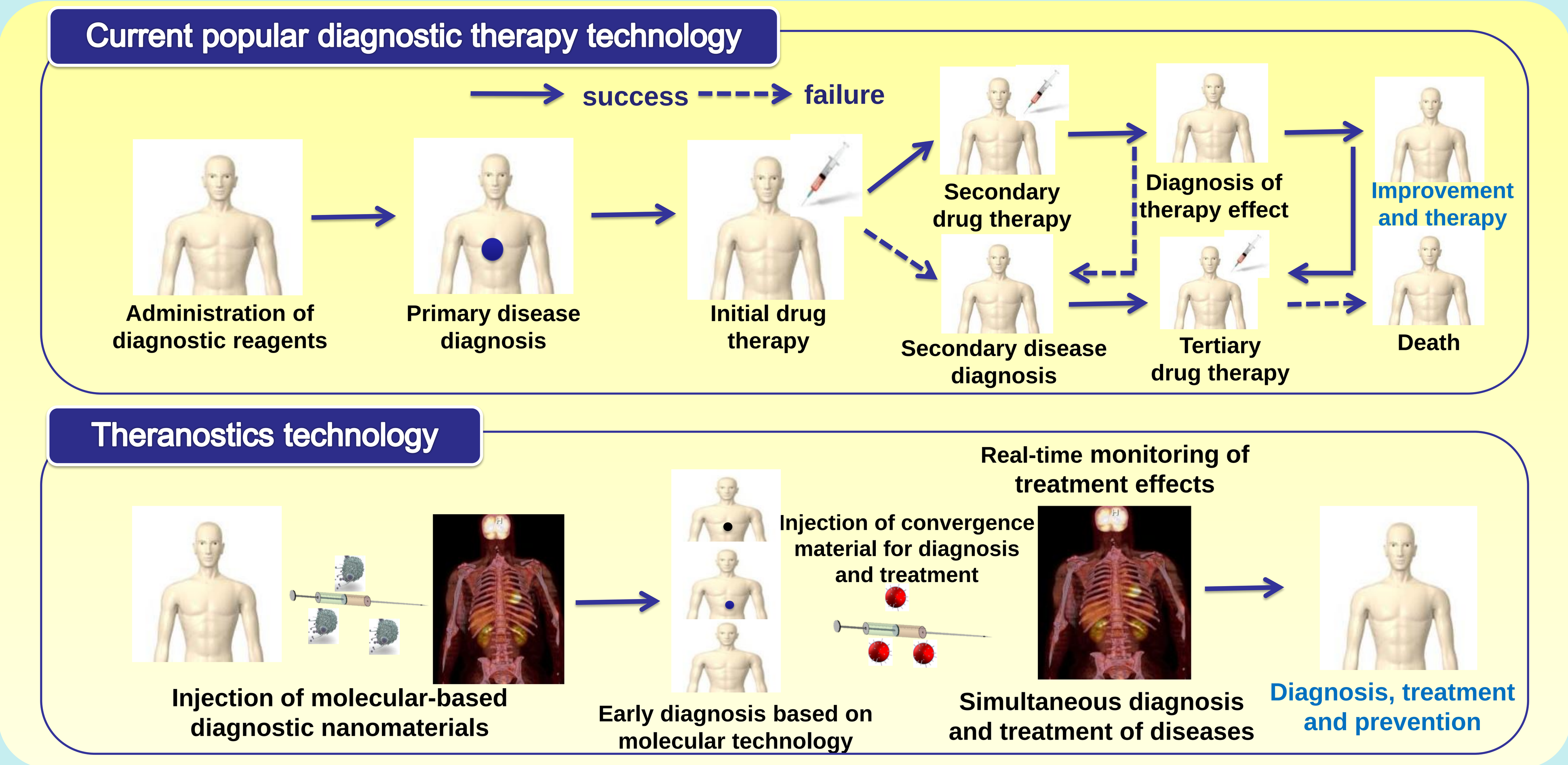
Introduction

As human life expectancy extends and interest in healthy living rises, social demands for innovative treatment technologies that can improve the "quality of life" of patients and their families are increasing [1]. As one of the key medical technologies for this purpose, theranostics (Theranosis = Therapy + Diagnosis), a new treatment technology that simultaneously performs diagnosis and treatment, is in the spotlight. Although the use of the term "Theranosis" has been relatively recent event, its concept is an conventional and safe, radiation therapy regimen, such as a diagnosis and concurrent treatment of thyroid disease using radioactive iodine. In addition, the emergence of theranosis suggested a new direction of development in the field of nuclear medicine to provide specific and personalized treatment for patients [2]. Theranostics is a new field of medical technology and requires further research for clinical application. In Korea, radiopharmaceuticals using medical radioisotopes, combined with nuclear medicine technology, are effective in the diagnosis and treatment of intractable diseases(cancer, brain diseases, etc.), and the production and research base are rapidly growing.

Fig. 1. Direction of future medicine: The 4P precision medicine.



Production of Radioisotopes

Domestic production of radioisotopes for medical use comes from Hanaro, a multi-purpose reactor with 30MW. It is a great support in the supply of medical RI in Korea by producing ^{99m}Tc, ^{131}I, ^{153}Sm, ^{166}Ho and ^{90}Y. Many medical isotopes have been available by the distribution of Cyclotrons through National policy implementation. Since the construction of a non-powered research reactor with 15 MW(thermal neutron flux: 3×10^{14} n/cm^2 · s) of planned isotope production, research facilities and neutron research facilities, which will be completed within a few years, is under construction in Busan's Gijang-gun. It will play an important role in domestic production and distribution of isotope as well as creating research environment [3].

Fig. 2. Aerial view of a research reactor in Gi-jang

Table. 1. Production of theranostic radioactive isotopes capable of simultaneous diagnosis and treatment

Source	Radionuclide	Nuclear reaction	
Reactor	^{131}I	$^{235}U(n, fission)^{131}I$ or $^{130}Te(n, \gamma)^{131}Te \xrightarrow{\beta-} {}^{131}I$	
	^{67}Cu	$^{67}Zn(n, p)^{67}Cu$	
	^{177}Lu	$^{176}Lu(n, \gamma)^{177}Lu$	
	^{186}Re	$^{185}Re (n, \gamma)^{186}Re$	
	^{153}Sm	$^{152}Sm (n, \gamma)^{153}Sm$	
	^{47}Sc	$^{46}Ca(n, \gamma)\,^{47}Ca \xrightarrow{\beta-} {}^{47}Sc$	
Cyclotron	^{64}Cu	$^{64}Ni(p, n)^{64}Cu$	
Generator	^{188}Re	$^{187}W(n, \gamma)^{188}W \xrightarrow{\beta-}_{69.4d} {}^{188}Re$	$^{188}W\rightarrow{}^{188}Re$ generator
	^{90}Y	$^{235}U(n, fission)^{90}Sr \xrightarrow{\beta-}_{28.8yr} {}^{90}Y$	$^{90}Sr\rightarrow{}^{90}Y$ generator

Theranostic Radioisotopes

Radioisotopes used for diagnosis and treatment should emit beta rays, which are weak in permeability but strong in tissue destruction, and also emit gamma rays. In addition, radionuclides with appropriate half-lives should be used to make images which can be utilized for diagnosis during the treatment course. Furthermore, the most important factor in the development of radiopharmaceuticals is the selection of appropriate radioisotopes. Factors to be considered in the selection of such radioisotopes include radiation emission characteristics, physical half-life, decay, productivity, cost and convenience of radioisotopes by giving priority to in vivo characteristics of radiopharmaceuticals to be developed. As with other therapeutic radioisotopes, the practical considerations for the selection of treatment simultaneously are not only high radiochemical purity but also high non-radioactive label efficiency stability and convenience .

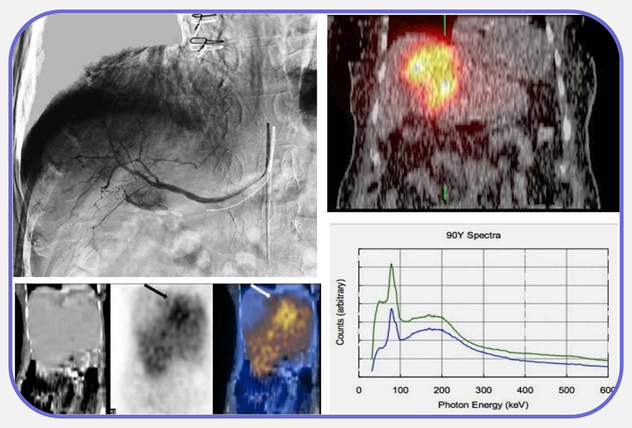


Fig. 3. ^{90}Y SIR-sphere therapy and Bremsstrahlung Imaging

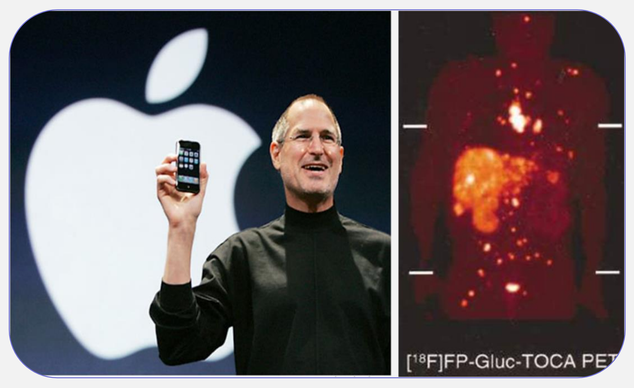


Fig. 4. ^{90}Y-DOTATOC (ONALTA) Neuroendocrine Cancer Treatment (PRRT) Steve Jobs received at the University of Basel, Switzerland (2009)

In order to develop effective therapeutic radiopharmaceuticals, the selection of the appropriate radioisotope is essential as well as suitable pharmacological aspects which can be integrated in the target region of the body to release desired therapeutic dose. Currently, ^{131}I, ^{64}Cu, ^{67}Cu, ^{186}Re, ^{177}Lu, ^{90}Y, etc. are used, and the development for the production of carrier-free RI; ^{177}Lu, ^{147}Pm, ^{47}Sc, ^{67}Cu, and generator technology for $^{188}W/^{188}Re$ and $^{90}Sr/^{90}Y$ are in process. In addition to radiopharmaceuticals widely used in domestic and overseas clinical fields, theranosis technology is being applied to various diseases using ^{131}I, ^{223}Ra, ^{90}Y, ^{177}Lu, etc (Table 2) [4].

Table 2. Established theranostic agents in current clinical use.

Clinical indication	Diagnostic agent	Therapeutic agent
Hyperthyroidism or thyroid cancer	^{123}I-iodide	^{131}I-iodide
Adrenergic tumors	^{123}I-iobenguane	^{131}I-iobenguane
Bone metastases from prostate cancer	^{99m}Tc-MDP	^{223}Ra chloride
Non-Hodgkins lymphoma	^{111}In-ibritumomab	^{90}Y-ibritumomab
Neuroendocrine tumors	^{68}Ga-DOTATATE	^{177}Lu-DOTATATE
Prostate cancer	^{68}Ga-DKFZPSMA-11	^{177}Lu-DKFZPSMA-617

Future Directions of Theranostic Radioisotopes

To make theranostics possible, it is essential to install non-power research reactors and install isotope accelerators to understand and develop radioisotopes which emit beta rays and gamma rays simultaneously. Numerous radiopharmaceuticals are already used in the treatment of intractable cancer, and the development of molecular target drugs, which are essential for medicines, is continuously increasing, raising the opportunity of developing radiopharmaceuticals for effective diagnosis and treatment. The key to achieve success of Theranosis technology is by developing nuclear medicine technology and radiopharmaceuticals through enhancing the production of isotopes and develop new isotopes to supply the medical market by collaborating with large research facilities that are capable of producing isotopes. Furthermore, government-level supply and demand systems for radiopharmaceuticals and support for researcher's development of production technology should be provided. Clinical application technology that enables diagnosis and treatment at the same time is a breakthrough technology that can increase cancer cure rate and reduce patient discomfort without time difference between diagnosis and treatment, leading the future knowledge-based industry as a core business of high value-added advanced medical industry that can be a future strategic field for improving the public health. However, in order to achieve such development, preparing a new govern-mental supply and demand system for radioisotopes and radiopharmaceuticals and supporting researcher's development of production technology is necessary.

References

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