Department of Innovative Interventional Endoscopy Research

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General Summary

This department was established in April, 2015, aiming at methodology of new endoscopic diagnosis and treatment, and also the development of apparatus, along with for the purpose of supporting and teaching to arrange the environment toward the standardization of endoscopic medicine not only in domestic but also in foreign facilities.

Research Activities

Endoscopic submucosal resection (ESD), which was developed in Japan, is followed by various improvements to conduct safely, promptly and accurately. Subsequently to ESD, new minimally invasive endoscopic treatments, such as endoscopic full thickness resection and endoscopic treatment applying robotic technology are being developed one after another. Now Japan is reaching an aging society at unprecedented speed among other countries, while its population is decreasing. Japanese world-class technology cultivated from experience of craftsmanship is a base for the development of endoscopy and even more growth is expected in the future. Especially minimally invasive endoscopic treatments with less burden to patients contribute significantly. While social demand for endoscopic medicine is growing, it is meaningful to propel new methodology for endoscopic treatment and development of instruments for it.
This department plays a role, in addition to the study of the above, to support formulation of educational structure of endoscopy for the doctors not only in Japan but in Asia, Russia, Middle East, and South America.

Development of supporting devices for ESD and clinical evaluation
One of the problems of the oral and transanal endoscopic therapy such as ESD is that only the skilled doctors can conduct them safely. Existing surgical instruments are electric scalpels, piercing through the forceps at its entrance of about 2.8 mm in diameter to penetrate a flexible endoscope, which move only to-and-fro. It makes extremely difficult to lift an affected part and cut the inside open while operating a fiberscope minutely with all these devices. The endoscopic system, which can operate by two hands of right and left to move freely, has been expected for long time, and an elasticity forceps to bend have been researched and developed all over the world. But they are not practical since the current smallest ones were 4mm in diameter so far, not being able to insert in the forceps channel (2.8 mm) of the existing elasticity endoscope. An article specially made to order costs expensive. Since a flexible endoscope is expensive, it is a medical condition to make ends meet economically to develop one which can be used daily. Because a forcep's outlet of flexible endoscope commercially available is around 3 mm in diameter, a flexible forcep

of around 2.6 mm in diameter is necessary to insert. The flexible flexure forceps of 2.6 mm in diameter was succeeded (Nakadate R et al. Endoscopy 2015; 47(9): 820–4). This promoted appearance of medical device for practical use which may make ends meet economically. Furthermore, in consideration for utility and economy, two control sticks are equipped to the fixed base to be manipulated stable, and a grip of flexible scope and its console are placed as can be reached at the same time so one endoscopist can conduct procedure. The flexible endoscopes can be removed anytime for manual manipulation when it is necessary. Besides they are robotic devices not requiring motors, which make them as nearest as practical application. We have been repeating animal studies of in vivo, ex vivo and evaluated their clinical usefulness. We will continue to work on the technological development for conducting ESD without stress.

Endoscopic optical molecular imaging for cancer

Molecular targeted therapies, such as monoclonal antibodies, were widely used for various cancers recently, leading to improve patients' outcomes. Use of the molecular targeted medicine for cancer patients generally depend on the level of molecular expression in the targeted tumor, therefore, developing a method of companion diagnosis is required at the same time of developing a molecular-targeted therapy. We have developed a method of molecular target-specific fluorescence cancer imaging and phototherapy, called photoimmunotherapy. To expand the applicability of photoimmunotherapy, we developed a novel photoactivatable bifunctional antibody-drug conjugate that can work as both photoimmunotherapy and chemoimmunotherapy agents. We evaluated the feasibility of IR700 conjugated trastuzumab emtansine (T-DM1-IR700)-mediated near-infrared light irradiation by comparing the in vitro and in vivo cytotoxic efficacy of trastuzumab-IR700 (T-IR700)-mediated NIR light irradiation in HER2-expressing cells. In vivo photoimmunotherapy using T-DM1-IR700 did not show a superior antitumor effect to photoimmunotherapy using T-IR700 in subcutaneous small-tumor models, which could receive sufficient near-infreared light. In contrast, photoimmunotherapy using T-DM1-IR700 tended to reduce the tumor volume and showed significant prolonged survival compared to photoimmunotherapy using T-IR700 in large-tumor models that could not receive sufficient near-infrared light.

Currently, phase 2 clinical study is ongoing for recurrent head and neck cancer patients in multiple US sites. This method could serve as an aid for expanding the indication of photoimmunotherapy.

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