Here begins our new MIRAI
MOONSHOT RESEARCH & DEVELOPMENT PROGRAM

R&D Item

3. Health and Medical Demonstration with In-Body CA

Progress until FY2024

1. Outline of the project

In this R&D Item, we will design prototypes of in-body cybernetic avatar(in-body CA) with distributed teleoperation (distributed CA) and in-body CA with cooperative teleoperation (cooperative CA). We will clarify demonstration issues, conduct experiments, and verify the effectiveness. We will also identify problems related to Ethical, Economic, Environmental, Legal, and Social Issues (E^3LSI) corresponding to the application examples and show how to solve them.

2. Outcome so far

From a medical perspective, we classified the multitasking processes required for cooperative CA and examined the elemental technologies. The required elemental technologies included driving function, moving function, operating function, cooperative function, measuring function, communication function, power supply function, medication function, transport function, and presentation function (visual, force, tactile).

Among these elemental technologies, we verified the operation and cooperative functions required for "collection of tissue, cells, bacteria, etc. from abnormal sites," previously listed as a multitasking process. Using the traction device, which simulates in-body CA, we showed that it is possible to shorten the time and improve the safety of tissue collection for living pigs and humans. The issues, techniques, and other findings obtained here can be reflected in the design of the cooperative CA. In-body CA is also considered useful in processes such as observing abnormal sites, diagnosing collected specimens, and repairing collected sites.

Concerning distributed CA, promising genetic markers for detecting abnormalities and findings on bacterial flora have been obtained, and analysis of the effects of pH changes in the body is in progress.

The following findings regarding promising genetic markers to be measured have been made.

- We analyzed metabolites in gastric cancer mucosa and confirmed that 107 metabolites significantly differed from the surrounding healthy mucosa. One of the metabolites, Prostaglandin E2 (PGE2), was shown to be a potential marker for the detection of gastric cancer.
- We analyzed gene expression in the colonic mucosa of patients intolerant to therapeutic agents for inflammatory bowel disease. We identified genes whose expression was specifically upregulated in the colonic epithelial cells of patients intolerant to therapeutic drugs.

The following findings emerge regarding the association between bacterial flora and health status.

- Bacterial flora (increased Fusobacterium) is associated with papillary tumor progression.
- Short-chain fatty acid-producing bacteria in stool are increased in patients with chronic hepatitis B who have achieved functional cure.
- Treatment of inflammatory bowel disease improves intestinal microbiota dysbiosis.

We also measured pH in bile and found that pH tended to differ in cases of common bile duct stones depending on the presence or absence of cholangitis. We have developed a temporal pH measuring device and can now continuously measure the pH of bile in actual cases for a continuous period of 31 hours. We will investigate the relationship between diet, medication, and other factors and pH.

Regarding evaluating stent-type in-body CA, we conducted animal experiments using living pigs to validate a bile duct stent CA prototype containing a small pH sensor.

Regarding medication, small animal experiments have shown that the efficacy of anticancer drugs is increased by oral administration of alkalizing agents. We are working to elucidate the mechanism, focusing on cancer-associated fibroblasts.

As for capsule-type in-body CAs, we are developing a manufacturing technology that can guarantee safety and high quality in preparation for conducting clinical trials to administer in-body CA specialized for measuring deep body temperature and its temporal fluctuations to humans for the first time. One of these is encapsulation technology using biocompatible resin, and we have developed a mass production technology for encapsulation by insert molding (Figure 1). As a result of test molding, normal operation was confirmed. We consider this achievement a significant step toward the social implementation of in-body CA.

We identified further issues considering the review report on capsule endoscopes and other products. We discussed a plan to overcome them regarding safety standards and environmentally friendly design that should be observed when these technologies are installed in products, as well as E^3LSI issues that may arise when implemented in society.

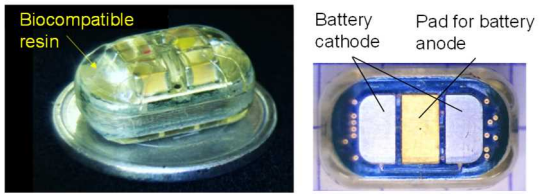

Figure 1: Capsule-type In-body CA Using Biocompatible Resin

3. Future plans

We will strongly cooperate with R&D thema 1, 2, and 4 and promote demonstration experiments. We will also identify corresponding E^3LSI issues and promote R&D regarding social implementation.

JST Japan Science and Technology Agency