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Fluorescent Imaging

Treatment of Hepatobiliary and Pancreatic Diseases

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34 figures, 23 in color, and 8 tables, 2013
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I do not recall the exact date, but I clearly remember how excited we were to find an ‘illuminated’ liver tumor in the OR one day in 2007. It was several weeks later that we started a prospective study on intraoperative ICG fluorescence cholangiography during liver surgery. We injected 100-fold diluted ICG solution via a tube inserted into the cystic duct to obtain anatomical information on the biliary tree. The patient had a recurrent hepatocellular carcinoma (HCC). Following cholecystectomy and insertion of a C-tube, we applied a near-infrared camera for fluorescence cholangiography. Immediately after the intrabiliary injection of ICG, we could identify the biliary tree, as expected. At the same time, however, we also found that the tumor itself was illuminating! Wait a second, has the tumor not been fluorescing from before the injection of ICG into the cystic duct? Instantly, we realized that the fluorescence of the tumor originated, in all likelihood, not from the ICG that we injected intraoperatively into the cystic duct, but from the ICG that we had injected 1 week before the operation as part of preoperative liver function testing.

It was then quite natural for liver surgeons to hypothesize that HCC cells can also take up ICG, just like hepatocytes, from which they arise. Normal hepatocytes quickly excrete ICG into the bile, so that they no longer illuminate fluorescence 1 week after the ICG injection. On the other hand, in the case of HCC cells, possibly on account of the disturbed excretory function of the cells, ICG excretion may be impaired and the ICG may be retained for weeks in the HCC cells. So far, evidence supports this aforementioned hypothesis, and molecular analyses on the genes encoding the transporters of this dye may help in a clearer elucidation of this phenomenon in the near future.

ICG is an old friend for hepatobiliary surgeons. It received FDA approval for clinical use more than half a century ago, and has been a very useful dye for liver function testing. ICG fluorescence angiography was applied first for visualizing the retinal artery by ophthalmologists in the late 1960s. It was then applied to the study of cerebral arteries, coronary arteries, limb arteries, mesenteric arteries, etc. With recent advances in imaging technologies, ICG has received renewed attention in the field of hepatobiliary surgery as a new tool for visualizing the biliary tree and liver tumors. What is unfortunate for this very useful dye in medicine, however, is that it is very cheap.
and is available for only JPY 644 (approximately USD 6.33 or EUR 4.89) for a 25-mg vial. The price is so low that no pharmaceutical company in the world has shown any interest in conducting expensive clinical trials to expand the clinical indications for the use of ICG.

This book on fluorescence imaging in the field of hepatobiliary and pancreatic diseases introduces cutting-edge knowledge about the exciting imaging technique using ICG and other new promising chemicals. I would like to thank all of the contributors for sharing their latest findings. I hope this book will encourage not only researchers, but also entrepreneurs, to promote technical developments and popularization of this technology. Lastly, I would like thank Dr. Takeaki Ishizawa, the co-editor of this book and a brilliant colleague of mine, as well as S. Karger Medical and Scientific Publishers for their energetic work in publishing this wonderful book.

_Norihiro Kokudo, MD, PhD, Tokyo_