

Fluorescent Imaging: Treatment of Hepatobiliary and Pancreatic Diseases

Frontiers of Gastrointestinal Research

Vol. 31

Series Editor

Choitsu Sakamoto Tokyo



Fluorescent Imaging

Treatment of Hepatobiliary and Pancreatic Diseases

Volume Editors

Norihiro Kokudo Tokyo

Takeaki Ishizawa Tokyo

34 figures, 23 in color, and 8 tables, 2013

KARGER

Basel · Freiburg · Paris · London · New York · New Delhi · Bangkok ·
Beijing · Tokyo · Kuala Lumpur · Singapore · Sydney

Frontiers of Gastrointestinal Research

Prof. Norihiro Kokudo, MD, PhD

Professor and Chairman
Hepato-Biliary-Pancreatic Surgery Division
Artificial Organ and Transplantation Division
Department of Surgery, Graduate School of
Medicine
The University of Tokyo
Tokyo 113-8655
Japan

Dr. Takeaki Ishizawa, MD, PhD

Assistant Professor
Hepato-Biliary-Pancreatic Surgery Division
Artificial Organ and Transplantation Division
Department of Surgery, Graduate School of
Medicine
The University of Tokyo
Tokyo 113-8655
Japan

Library of Congress Cataloging-in-Publication Data

Fluorescent imaging: treatment of hepatobiliary and pancreatic diseases /
volume editors, Norihiro Kokudo, Takeaki Ishizawa.

p. ; cm. -- (Frontiers of gastrointestinal research, ISSN 0302-0665
; vol. 31)

Includes bibliographical references and indexes.

ISBN 978-3-318-02292-6 (hard cover : alk. paper) -- ISBN 978-3-318-02293-3
(electronic version)

I. Kokudo, Norihiro, editor of compilation. II. Ishizawa, Takeaki, editor
of compilation. III. Series: Frontiers of gastrointestinal research ; v. 31.
0302-0665

[DNLM: 1. Biliary Tract Diseases--surgery. 2. Liver Diseases--surgery.

3. Digestive System Surgical Procedures--methods. 4. Optical
Imaging--methods. 5. Pancreatic Diseases--surgery. W1 FR946E v.31 2013 /
WI 770]

RD546

617.5'56--dc23

2013019195

Bibliographic Indices. This publication is listed in bibliographic services, including Current Contents® and Index Medicus.

Disclaimer. The statements, opinions and data contained in this publication are solely those of the individual authors and contributors and not of the publisher and the editor(s). The appearance of advertisements in the book is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality or safety. The publisher and the editor(s) disclaim responsibility for any injury to persons or property resulting from any ideas, methods, instructions or products referred to in the content or advertisements.

Drug Dosage. The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved. No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

© Copyright 2013 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)

www.karger.com

Printed in Germany on acid-free and non-aging paper (ISO 9706) by Kraft Druck, Ettlingen

ISSN 0302-0665

e-ISSN 1622-3754

ISBN 978-3-318-02292-6

e-ISBN 978-3-318-02293-3

Contents

VII Preface

Kokudo, N. (Tokyo)

History and Basic Technique of Fluorescence Imaging for Hepatobiliary-Pancreatic Surgery

1 History and Basic Technique of Fluorescence Imaging for Hepatobiliary-Pancreatic Surgery

Ishizawa, T.; Kokudo, N. (Tokyo)

Clinical Applications of Indocyanine Green Fluorescence Imaging

10 Identification of Hepatocellular Carcinoma

Ishizawa, T.; Kokudo, N. (Tokyo)

18 Identification of Metastatic Liver Cancer

Lim, C. (Créteil); Vibert, E. (Villejuif)

25 Identification of Occult Liver Metastases

Yokoyama, N.; Otani, T. (Niigata)

33 Application of Fluorescence Imaging to Hepatopancreatobiliary Surgery

Hutteman, M.; Verbeek, F.P.R.; Vahrmeijer, A.L. (Leiden)

42 Applications of Indocyanine Green Fluorescence Imaging to Liver Transplantation

Kawaguchi, Y.; Ishizawa, T.; Sugawara, Y.; Kokudo, N. (Tokyo)

49 Staining of Liver Segments

Aoki, T.; Murakami, M. (Tokyo); Kusano, M. (Hokkaido)

58 Visualization of Cholecystic Venous Flow for Hepatic Resection in Gallbladder Carcinoma

Kai, K. (Himeji)

66 Fluorescence Cholangiography in Open Surgery

Mitsuhashi, N.; Shimizu, H.; Miyazaki, M. (Chiba)

73 Fluorescence Cholangiography in Laparoscopic Cholecystectomy: Experience in Japan

Tagaya, N.; Sugamata, Y.; Makino, N.; Saito, K.; Okuyama, T.; Koketsu, S.; Oya, M. (Koshigaya)

80 Fluorescence Cholangiography in Laparoscopic Cholecystectomy: Experience in Argentina

Dip, F.D.; Nahmod, M.; Alle, L.; Sarotto, L.; Anzorena, F.S.; Ferraina, P. (Buenos Aires)

- 86 Simultaneous Near-Infrared Fluorescence Imaging of the Bile Duct and Hepatic Arterial Anatomy for Image-Guided Surgery**
Tanaka, E. (Sapporo); Ashitate, Y. (Sapporo/Boston, Mass.); Matsui, A.; Narsaki, H.; Wada, H. (Sapporo); Frangioni, J.V. (Boston, Mass.); Hirano, S. (Sapporo)
- 92 Laparoscopic Fluorescence Imaging for Identification and Resection of Pancreatic and Hepatobiliary Cancer**
Bouvet, M.; Hoffman, R.M. (San Diego, Calif.)
- 100 Novel Fluorescent Probes for Identification of Liver Cancer and Pancreatic Leak**
Yamashita, S.; Ishizawa, T.; Miyata, Y.; Sakabe, M.; Saiura, A.; Urano, Y.; Kokudo, N. (Tokyo)
- 106 Novel Fluorescent Probes for Intraoperative Cholangiography**
Vinegoni, C.; Siegel, C.; Mlynarchik, A.; Sena, B.F. (Boston, Mass.); de Abreu, L.C. (Santo Andre); Filho, J.L.L. (Recife); Figueiredo, J.-L. (Boston, Mass.)
- 113 Endoscopic Examination Using Fluorescent Probes**
Goetz, M. (Tübingen)
- 121 Author Index**
- 122 Subject Index**

Preface

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 to 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