Pinghong Zhou
Liqing Yao
Xinyu Qin
Editors

Atlas of Digestive Endoscopic Resection

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Foreword 1

Digestive endoscopic resection techniques are undergoing rapid development in recent years. Among them, endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are renowned world widely nowadays. New emerging techniques have derived from ESD, for example, submucosal tunnel technique which includes peroral endoscopic myotomy (POEM) for the treatment of esophageal achalasia, and submucosal tunneling endoscopic resection (STER) for the treatment of upper gastrointestinal submucosal tumors. These minimally invasive surgeries not only provide effective treatment for early gastrointestinal carcinoma and submucosal tumors, but also benefit the patients financially. This fully reflects the advantage of "minimally invasive treatment".

Led by Prof. Liqing Yao, Prof. Pinghong Zhou's ESD treatment team from the Endoscopy Center, Zhongshan Hospital, Fudan University, have done a lot of work on early gastrointestinal carcinoma and submucosal tumors. Their team has been at the forefront in China as well as worldwide, with a remarkable number of both diagnostic and therapeutic endoscopy. They have attracted many international professionals to learn ESD and submucosal tunnel technique in their center. In recent years, their team focuses on ESD technique and tunnel technique as the discipline characteristic and main direction, continuously exploring and innovating in this field. They have become the trailbreaker in the development of new techniques in China. For example, STER was first innovated in this center, as I know. Currently, it has become the endoscopic training center of Asia-Pacific region.

Four years ago, the first edition of this book, also the first ESD monograph in China, played a positive role in promoting the development of ESD in China. I was honored to write the foreword for the very first edition. Once published, it was welcomed and highly praised by domestic and foreign counterparts. The second edition of this book was therefore emerged in 2012 and evoked strong repercussions in reading public. The 3rd edition (English version) of *Digestive Endoscopic Resection* consists of seven chapters. It is not only the extension of the contents in previous two editions, but also includes a large number of new cases, especially in tunneling endoscopy. This book may provide clinical endoscopists valuable experience for thorough implementation of endoscopic treatment, and also promote the communication between China and the world in this field.

I am fortunate to look through this book before publication and found the contents innovative with strong theoretical property and practicability. It is my pleasure to write the foreword for this book and recommend this it to those whose careers are involved in endoscopy.

William Chao
President, World Endoscopy Organization
President, Asia Pacific Society of Digestive Endoscopy
Hongkong, December, 2013

Foreword 2

Professor Pinghong Zhou is a person of great talents.

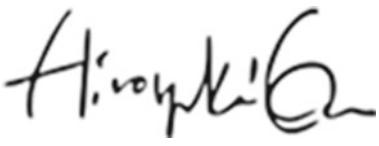
It was 1996 when Dr. Hosokawa, Dr. Gotoda and I, the Endoscopy Group at the National Cancer Center Hospital, Tokyo, Japan, first used the IT knife in endoscopic submucosal dissection (ESD) for early gastric cancer. It's unbelievable how fast the 18 years have passed since then.

I believe my first meeting with Professor Zhou was in the summer of 2006 while he was visiting the Shizuoka Cancer Center. We hit it off right away, and I was deeply impressed by his passion for endoscopic treatment. With his enthusiasm and talent, Professor Zhou became an ESD expert in no time, and subsequently became a pioneer of ESD in China. One of his great attributes is that he continually goes beyond improving his own skills and is committed to disseminating ESD among physicians across China. Successful ESD requires sound surgical skills, aptitude for early tumor detection and accurate diagnosis of tumor extension and depth, and knowledge about treatment indications. I respect Professor Zhou because, even through all the glitz and glamor that surrounds ESD technique, he understands that the significance of ESD is for us to accurately diagnose disease, and so he continues to educate himself in the field. I have participated in the Sino-Japan Summit Forum on ESD organized and managed by Professor Zhou since the first summit in 2007, and as a colleague in the same field, I am proud to see the immense contributions he makes, through his live demonstrations and lectures, to improve endoscopic treatment in China.

Today, Professor Zhou's work has expanded extensively to cover even per-oral endoscopic myotomy (POEM) and endoscopic full-thickness resection (EFTR), and his work is renowned worldwide. Yet, he continues to make ceaseless efforts to push to new frontiers.

I believe this atlas will be a great help to endoscopists wanting to master endoscopic diagnosis and treatment such as ESD. Let's join Professor Zhou in his work and together open up new possibilities for endoscopic therapy.

Hiroyuki Ono, MD, PhD
Medical Deputy Director of Shizuoka Cancer Center
Chief of Endoscopy Divsion, Shizuoka Cancer Center
Shizuoka, Japan



Foreword 3

Professor Pinghong Zhou contributed his great effort to improve the knowledge and skill of Chinese endoscopists through the textbook, the first Chinese version of Endoscopic Submucosal Dissection (ESD) and the live course, Shanghai International Endoscopy Symposium (SIES). Professor Zhou is the pride of all of us who are serving in this field.

Therapeutic endoscopy has changed dramatically since the end of the last century. Endoscopists' workplace is now moving from mucosa to the submucosal layer and deeper. This amazing innovation has carried a huge benefit as minimum invasive treatment to patients whose organs can be preserved. This field is still progressing day by day. The advance may completely break down the wall separating physicians and surgeons.

Hence, I believe that Professor Zhou, a surgeon, is now a hero of the times. Actually, Professor Zhou is an endoscopist who has experienced a greatest number of peroral endoscopic myotomy (POEM) for achalasia in a short period. This atlas comprehends recent advanced procedures. Moreover, I have been really impressed that Professor Zhou has not skipped the diagnostic chapter, which is the cornerstone of treatment for lesions of the gastrointestinal tract.

I do not know where we, endoscopists, are headed to. However, I can express that this atlas will be a milestone in the field of therapeutic endoscopy, and Professor Zhou will be able to conduct us to the destination of our journey.

Takuji Gotoda
Department of Gastroenterology and Hepatology
Tokyo Medical University
Tokyo, Japan

Preface

Five years ago, when we wrote the first Chinese version of **Endoscopic Submucosal Dissection** (**ESD**), it was the first attempt ever that Chinese endoscopists systemically introduced the ESD technique—from equipment to facilities, from surgical procedure to postoperative complications, and from staff training to nursing cooperation, sharing our experience in ESD treatment for gastrointestinal (GI) diseases, especially the early GI cancer. As a must-have reference book for starting ESD treatment, ESD was then only available in a couple of large tertiary-care endoscopy centers in China. The first ESD book has a good reputation among gastroenterologists and surgical endoscopists, following the sold-out copies of over 5000.

With the first Chinese version gaining in popularity, we published the second Chinese version, which was entitled *Digestive Endoscopic Resection* so as to update the new offshoots of ESD technique. However, it can never meet the ever-growing demands from our overseas readers. While traveling around for international conferences, I was touched to see several centers keeping my first ESD book in their bookshelves though doctors there could not read Chinese. I came up with the idea that I had to do the tough job of translating the Chinese version into English. Hence the English version.

The new book is based on both of the Chinese versions; however, it is not merely the literal translation of the two. It has become more concise, practical and illustrated. Organized into seven different chapters, the first two introduce the practical use of diagnostic methods before endoscopic resection and involved equipment. Chapter 3 describes the history of endoscopic resection and introduces endoscopic mucosal resection (EMR). Chapter 4 focuses on detailed coverage of ESD approaches in different sites. The last two chapters highlight the cutting edge of emerging offshoots based on ESD technique, including endoscopic full-thickness resection (EFTR), combined endoscopic/laparoscopic resection, peroral endoscopic myotomy (POEM) for achalasia, and submucosal tunneling endoscopic resection (STER) for submucosal lesions.

I thank Springer and all my colleagues, who have contributed to make the book come into being. In particular, I thank Dr. Mingyan Cai and Dr. Quanlin Li, my colleagues, for their dedicated efforts and enormous work during the whole editing process which lasted nearly one year. Special thanks also go to Dr. Sauid Ishaq for his huge contribution in editing in terms of polishing words, sentences and meanings to help us express ourselves properly and vividly. Without them and without all the contributing authors of each chapter,

this book could not be published so soon. Last but not least, I would like to thank my wife Ms. Ying Zhang for standing beside me throughout my career and editing this book. She has been my inspiration and motivation for continuing to move my career forward.

We hope this book can serve as an ideal reference for everyone involved in endoscopy, whether they be endoscopy trainees, established endoscopists, trainees nurses, nurses or technical staff.

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China, Dec. 2013

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1

1.1 Endoscopic Ultrasonography

1.1.1 Overview

An endoscopic ultrasonography (EUS) uses an endoscope with an ultrasound probe attached to create real time detailed pictures of internal organs and structures.

In 1980, Dunagnoey and Strohm pioneered the use of EUS and after over 30 years of development, EUS has been playing an extremely important role in the diagnosis and treatment of digestive system diseases.

Commonly used ultrasonic endoscopes include ultrasonic gastroscopes, ultrasonic duodenoscopes and ultrasonic colonoscopes as well as mini ultrasonic probes that is passed either through an endoscopic biopsy channel for the diagnosis of subtle digestive tract wall and submucosal lesions or inserted into biliary and pancreatic ducts through duodenal papilla to perform detailed examination. Therapeutic indication include EUS-guided fine needle aspiration. Recent combination of color Doppler imaging with EUS enhanced accuracy of imaging and enabled the scanning of arterial and venous blood flows. Advancement in technology has allowed and its gradual application in clinical practice.

1.1.2 Classification of Ultrasonic Endoscopes

1.1.2.1 Dedicated Ultrasonic Endoscopes

Such type of ultrasonic endoscopes refer to those special endoscopes equipped with a mini ultrasonic probe permanently attached to their tip that allows detailed examination of superficial and deeper layers of digestive tract as well as adjacent structures.

1.1.2.2 Transendosopic Miniature Ultrasonic Probes

Such probe is 2 mm in diameter and can be inserted through the biopsy channel of endoscope into the lumen or even passed into biliary of pancreatic duct through duodenal papilla (IDUS). Its frequency ranges from 12 to 30 MHz.

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1.1.2.3 Color Doppler Ultrasonic Endoscopes

Color Doppler enhances the capability of endosonography by visualizing the blood vessels in the digestive tract. It reduces risk of puncturing blood vessels during EUS-guided fine needle aspiration. It additionally help to assess vascular parameters of a lesion.

The integration of endoscopic color Doppler ultrasonography (ECDUS) with puncture-intended ultrasonic endoscopes are of the linear array scanning type, while some probes are of the central groove needle type. The advantage of such type of endoscopes is that they can clearly visualize the needle route as well as the blood vessels within the scanned area. In addition to diagnostic use, these are intended for therapeutic procedures such as aspiration biopsy and treatment of the biliary and cystic space-occupying lesions.

1.1.2.4 Puncture-Intended Ultrasonic Endoscopes

Such type of endoscopes is primarily intended for performing the EUS guided fine needle aspiration (EUS guided FNA) as well as paracentetic aspiration, injection, catheter drainage in digestive tract, liver or pancreas lesions.

1.1.2.5 3D-IDUS

Three dimensional IDUS (3D-IDUS) can enable the 3D imaging in gastrointestinal tract and biliary and pancreaticducts to further improve the resolution and diagnostic accuracy. 3D-IDUS is primarily intended for morphological visualization of the biliary duct and diagnosis of adjacent small tumors. The minimum section interval is 0.25 mm and the maximum sampling length is 40 mm.

1.1.3 Clinical Applications

1.1.3.1 TN Staging of Gastrointestinal Tumors

Generally, most of the tumors of the gastrointestinal tract can be easily diagnosed by conventional endoscopy, however, it is not possible to determine the depth of tumor infiltration or involvement of regional lymph node. The EUS allows TN staging of the digestive tract cancers hence provide guidance for the selection of appropriate treatment.

EUS help decide suitability of lesion for ESD treatment. ESD is only indicated for flat lesions and early cancers of the mucosa or SM1 layer (SM1) without regional lymph node metastasis. EUS can effectively determine the depth of lesion as well as involvement of regional lymph node.

Esophageal Carcinoma

EUS is reliably accurate (>80 %) in preoperative local staging of esophageal cancer and is considered superior to CT, MRI scan, in assessing depth of primary tumor infiltration. EUS is also reliable in staging a tumor and detecting mediastinal lymph or node metastasis (Fig. 1.1). Currently, EUS is the most accurate non-operative technique to determine the depth of tumor invasion. EUS can accurately predict whether esophageal cancer can be completely resected hence guiding appropriate treatment.

In case of an early esophageal cancer, EUS can differentiate whether the lesions are mucosal or infiltrate into the submucosa or muscularis propria. This provide the basis for minimally invasive endoscopic resection for mucosal lesion if no regional lymph nodes are involved.

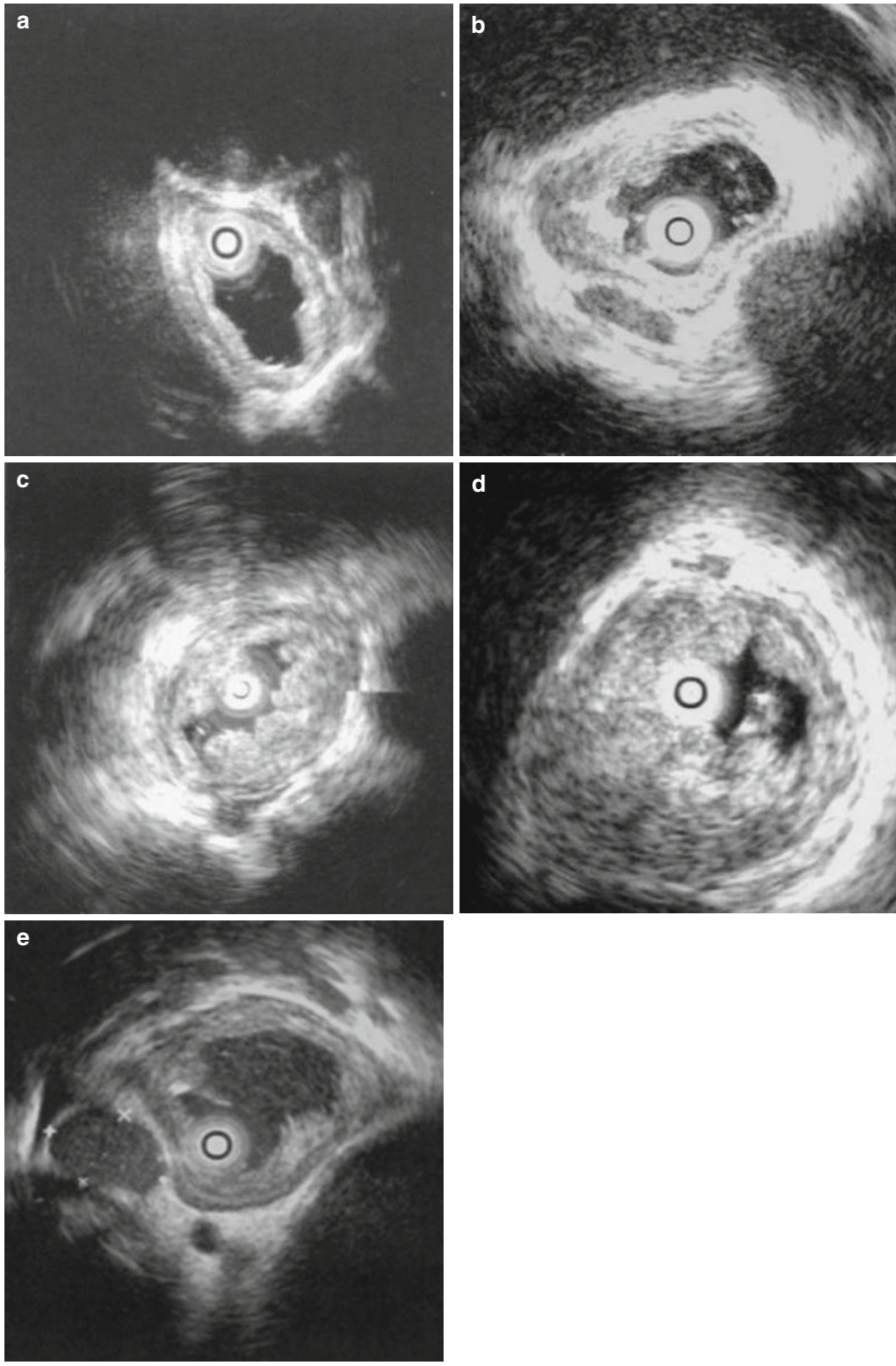

Fig. 1.1 TN staging of esophageal cancer by EUS. (**a**) Layer 1 is involved, Layer 2 is deficient and Layer 3 is partially invaded; (**b**) Layer 4 is slightly thickened and Layer 5 is not invaded; (**c**) The thickness of the esophageal wall is increased, but Layer 5 is intact; (**d**) Layer 5 is invaded; (**e**) Regional lymph nodes (+)

Gastric Carcinoma

Intramucosal cancers without lymph node metastasis are increasingly resected endoscopically. Long-term follow-up data indicates that endoscopic therapy can achieve the same effects as surgical resection but with fewer complications. Therefore, preoperative staging prior to an endoscopic treatment is extremely important. EUS is extremely helpful in differentiating mucosal tumors from tumors invading the submucosa. EUS finding of involvement of Layer 3 of the gastric wall, is indicative of submucosal invasion hence surgical resection is indicated. EUS is relatively good in assessing I and IIc lesions, but is far from perfect to stage IIa type of lesions.

EUS can reliably stage a gastric cancer in terms of the depth of tumor invasion to the gastric wall, affected adjacent lymph nodes and direct infiltration to the adjacent organs (Fig. 1.2).

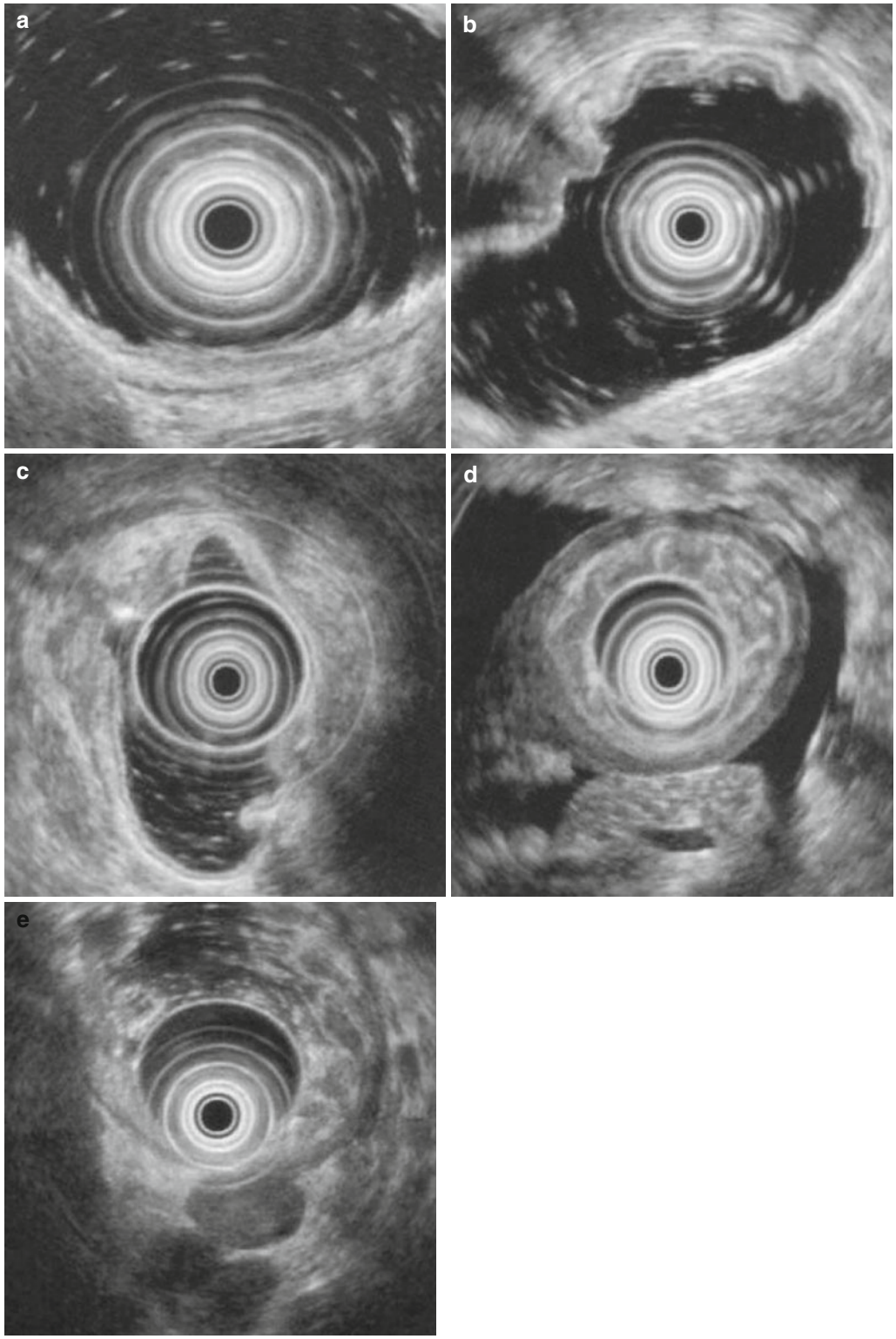

Fig. 1.2 TN staging of gastric cancer by EUS. (**a**) Early gastric cancer, hypoechoic and not penetrate the submucosa; (**b**) BorrmannII gastric cancer (fungating); (**c**) BorrmannIII gastric cancer (ulcerated); (**d**) BorrmannIV(infiltrating) gastric cancer, the gastric wall is significantly thickened, with structure destructed and ascitic fluid seen around the gastric wall; (**e**) Tumors have metastasized to the lymph nodes adjacent to the gastric wall

Colorectal Carcinoma

Flat lesions and early colorectal cancers are now treated with minimally invasive endoscopic therapy. EUS is being increasingly used in staging of colorectal cancer (Fig. 1.3). In case of low rectal cancer, preoperative EUS can determine the depth of tumor infiltration and whether adjacent organs have been invaded, thus providing information whether tumor can be resected and anus can be preserved. In case of early colorectal cancer, EUS can help determine lesions depth (infiltrated into the submucosa) to provide basis for suitability to select the minimally invasive endoscopic therapy.

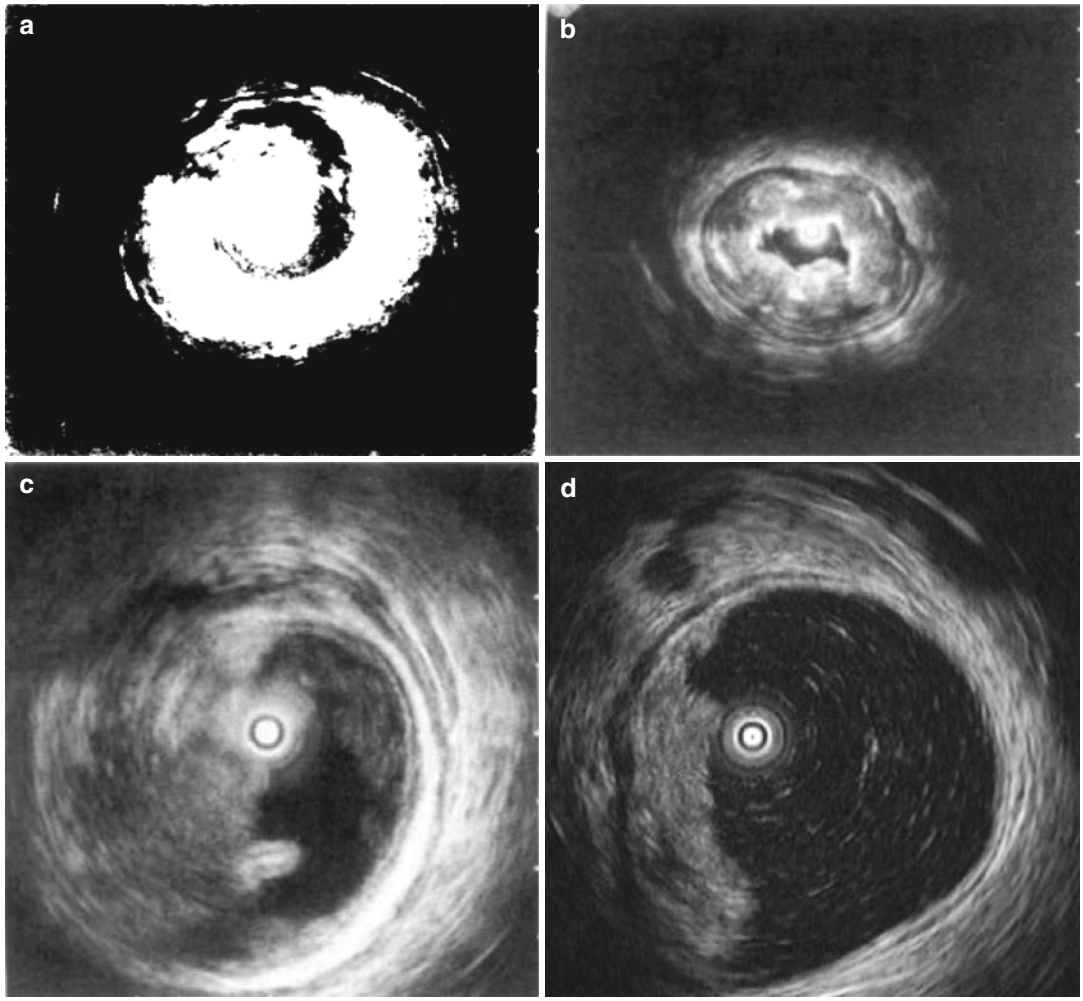

Fig. 1.3 TN staging of colorectal cancer by miniature EUS probe. (**a**) Tumors have affected Layer m and sm; (**b**) Tumors have affected Layer mp; (**c**) Tumors have affected the whole colonic layer; (**d**) Tumors have metastasized to the lymph nodes adjacent to the intestinal wall

1.1.3.2 Diagnosis of Gastrointestinal Submucosal Tumors

EUS can accurately assess submucosa tumors (SMTs) location, size and the layer of origin, and can also help characterize these lesions (Fig.1.4). Hypoechoic lesions derived from the muscularis mucosa (MM) or muscularis propria (MP) are either gastrointestinal leiomyoma or stromal tumors. Cysts, heterotopic pancreas and lipoma are derived from the submucosa. Carcinoid tumors, eosinophilic granuloma, myoblastoma, scarcoma, are less common. Feature suggestive of Lipoma is hyperechoic shadow, whilst cyst is indicated by well-defined anechoic shadow. Heterotopic pancreas is either hyperechoic or hypoechoic and granular in shape and sometimes can grow transmuraly. Tissues/fluid aspirated by EUS-guided puncture can be used for pathological and immunohistochemical examinations to establish the diagnosis.

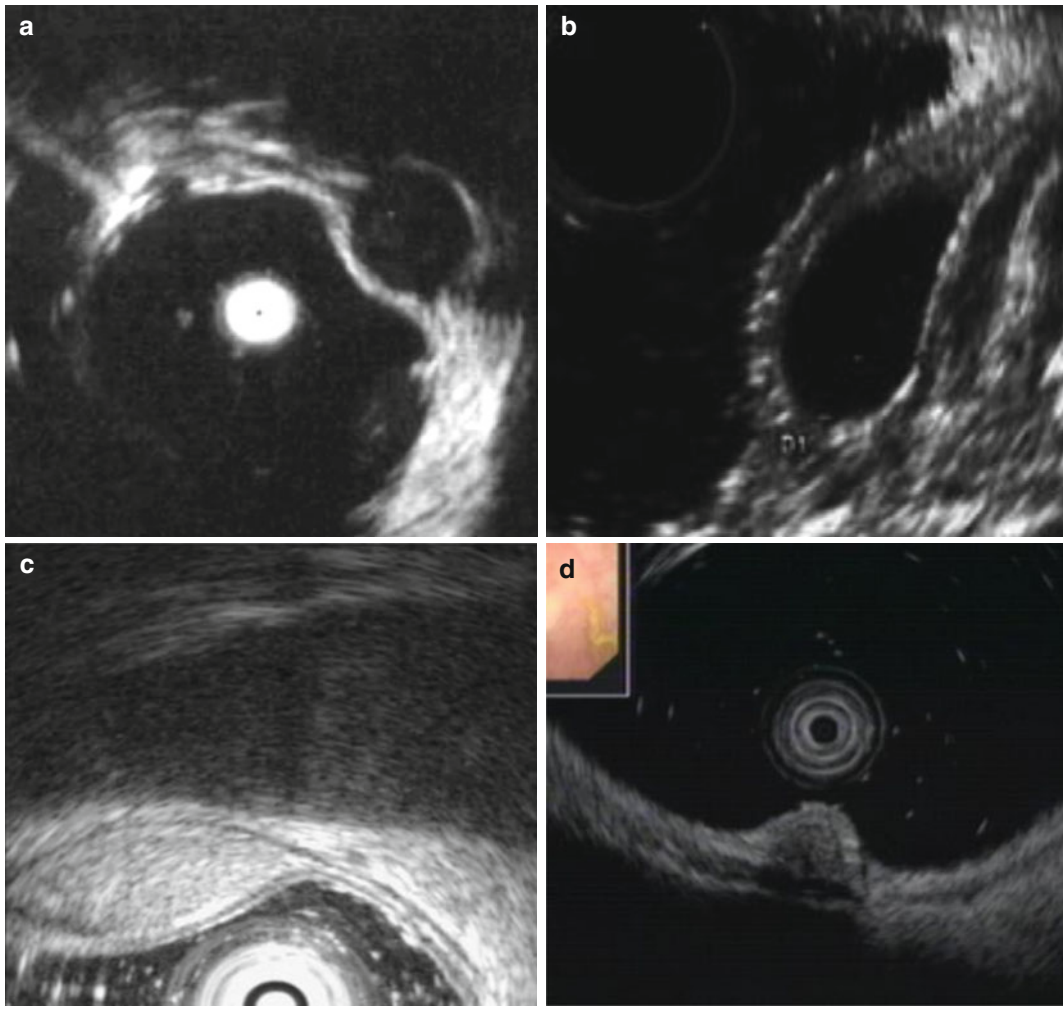

Fig. 1.4 Diagnosis of SMTs of large intestine by EUS. (**a**) Rectal stromal tumor or leiomyoma, derived from MP is hypoechoic; (**b**) Colonic cyst, derived from the submucosa is anechoic; (**c**) Colonic lipoma, derived from the submucosa is hyperechoic; (**d**) Rectal carcinoid, derived from the muscularis mucosa is heterogeneously echoic

EUS can determine the digestive tract wall layer from which the SMT is derived and this is critical in deciding suitability for endoscopic or surgical treatment. Over the recent years, by using the ESD technique we have successfully resected such various SMTs stromal tumor, leiomyoma, lipoma, glomus tumor, carcinoid, heterotopic pancreas and including tumors originating from MP.

1.1.3.3 Pancreato-Biliary System

Pancreas

EUS probe can be inserted through endoscope into duodenum to obtain ultrasonic image of the duodenal wall, duodenal papilla and periampulla. Five-layers of the duodenal wall can easily visualized that help to characterize whether a tumor is derived from the duodenal wall or periampullary area. Intraductal EUS (IDEUS) can be directly inserted into the pancreatic duct through the duodenal papilla to obtain clear images of the pancreas and peripancreatic area.

EUS is more sensitive than other imaging methods in assessing pancreatic tumors <2 cm in size. The diagnostic yield of pancreatic parenchymal tumors location and EUS guided fine needle aspiration (FNA) is relatively high. The sensitivity of EUS (98 % [95 % CI, 91–100 %]) for detecting a pancreatic mass is greater than that of CT (86 % [CI, 77–93 %]; P = 0.012). For the 53 surgical patients, endoscopic ultrasonography was superior to CT for tumor staging accuracy (67 % vs. 41 %; P < 0.001) but equivalent for nodal staging accuracy [1].

Pancreatic endocrine tumors can be either single or multiple with special biological behaviors. Most common examples are pancreatic islet cell tumors and ulcerogenic islet tumors. Generally, a pancreatic endocrine tumor can be detected when it is very small in size and over 90 % of them are smaller than 2 cm in diameter and well-defined with a hypoechoic structure. Endoscopic ultrasonography (EUS) offers a higher sensitivity (93–100 %) for detection of small potentially curable pancreatic masses when compared with existing imaging modalities [2].

EUS is relatively accurate in diagnosing chronic pancreatitis, comparable with ERCP, but better than CT scan. EUS can also give additional information such pancreatic stones and pancreatic duct dilation that may be accompanied by pancreas atrophy, local pancreatic enlargement or pseudocysts.

Biliary Tract Diseases

EUS is better that traditional abdominal US in obtaining higher resolution images because between the EUS probe and biliary system there is only a digestive tract wall.

EUS is accurate in diagnosing small tumors of the biliary system and enables assessment of depth of tumor infiltration. In addition detection of the adjacent lymph nodes by EUS in combination with the EUS-guided FNAB is high. In the assessment of bile duct cancer, it also provides additional staging information, whether portal vein, hepatic artery, head of pancreas and duodenal wall are invaded by the tumor. A miniature ultrasonic probe can be inserted into the bile duct that allows accurate diagnosis (early vs progressive) of the proximal bile duct tumors with high sensitivity and specificity. Preoperative and postoperative intraductal ultrasonography can assess bile duct cancer response to intraductal irradiation.

EUS is accurate to assess the depth of bile duct cancer infiltration. Traditional abdominal ultrasonography visualizes the gall bladder wall to a homogeneous and thin one-layered structure, while EUS visualizes the gall bladder wall to a three-layered structure by scanning through the duodenal bulb. Malignant lesions of the gall bladder wall are usually accompanied by the interruption or destruction of the continuous structure of the gall bladder wall, so the depth of infiltration by malignant lesions and whether such lesions have invaded into the liver can be determined by EUS.

EUS and IDEUS can clearly visualize the distal common bile duct and its contents hence has the advantage of diagnosing concurrent choledocholithiasis if present. Endoscopic ultrasonography has been proved to be of great sensitivity (up to 97 %) in the diagnosis of tiny stones that can be easily masked by contrast medium during ERCP, without any procedure-related complications and with a negative predictive value reaching 100 % [3].

1.1.3.4 EUS-Guided Fine Needle Aspiration Biopsy

EUS-guided fine needle aspiration (EUS-guided FNA) refers to a procedure in which a dedicated puncture needle is accurately advanced to the target under the real-time imaging and guidance by the ultrasonic probe mounted at the end of the ultrasonic endoscope and then fine needle aspiration of lesions is performed to conduct the pathological examination. Currently, the EUS-guided FNA technique has been applied in the diagnosis and treatment of lesions from areas such as gastrointestinal tract, mediastinum, lung, etc.

There are two types of EUS probes commonly used for puncture: linear array scan probes and rotating sector scan probes. The most commonly used probe is of the linear array type, which scans in a direction parallel to the needle route and can clearly visualize the needle route. In clinical application, different types of ultrasonic endoscopes are selected depending on the treatment purposes.

Role of EUS-FNA in Diagnosing SMTs

A SMT refers to a lesion between the deep mucosa and deeper serosa, more exactly, should be called "subepithelial lesion". After a suspicious SMT is found, the nature of that SMT should be further characterized. EUS can make a definitive diagnosis of a typical lipoma, and cyst, but cannot offer tentative diagnosis in the case of a hypoechoic lesions. In such cases EUS-FNA deep biopsy usually is required to confirm the diagnosis.

Role of EUS-FNA in Diagnosing Pancreatic Lesions

EUS-FNA is relatively accurate in diagnosing pancreatic cancer and about 10 % of the patients with distant lymph node metastasis and peritoneal or hepatic metastasis can be diagnosed by EUS-FNA which cannot be detected by other imaging modalities. If the results of the preliminary biopsy or initial EUS-FNA of a highly suspected pancreatic cancer are unclear or negative, another EUS-FNA procedure may be performed to increase the diagnostic accuracy.

In addition EUS-FNA can obtain cystic fluid samples for exfolicocytology, amylase, and tumor marker analyses (carcinoembryonic antigen). The increase of CEA level in cystic fluid favors the diagnosis of potential malignant mucous cyst lesions.

Role of EUS-FNA in Diagnosing Esophageal Cancer

In the lymph node staging in patients with esophageal cancer, EUS-FNA is more accurate than EUS and spiral CT. In the TN staging in patients who will undergo surgical resection procedure, EUS-FNA is more accurate so as to help the clinicians select the treatment protocol. Studies show that EUS-FNA is more accurate in the lymph node staging than FDG-PET CT.

Role of EUS-FNA in Diagnosing Gastric Cancer

In comparative studies, EUS generally provides a more accurate prediction of T stage than CT does. EUS-guided fine needle aspiration of suspicious nodes and regional areas adds to the accuracy of nodal staging. The routine use of staging EUS can sometimes alter the therapeutic plan because of the finding of otherwise occult distant metastases. About 8–15 % of the patients with gastric cancer who undergo EUS-FNA can have distant metastasis undetected by other imaging studies, hence influence treatment protocols [4]. We recommend that all of the patients with gastric cancer who are suspected to having distant metastasis should undergo FNA examination at the same time of EUS.

Role of EUS-FNA in Diagnosis of Rectal Cancer

Although EUS alone and EUS-FNA are not significantly different from each other in staging of rectal cancer, EUS-FNA can help visualize whether rectal cancer recurs. Therefore, EUS-FNA is not commonly used for the TN staging of rectal cancer but usually used for diagnosing the recurrent lesions.

1.1.3.5 Interventional EUS

Endosonography-Guided Cholangiopancreatography and Internal Drainage

EUS-guided cholangiopancreatography (EGCP) is a EUS-guided FNA technique which is primarily intended for evaluating the severity of pancreaticobiliary stenosis in patients if MRCP (fail to) detect biliary duct lesions ideally and ERCP is failed. EUS-guided cholangio-pancreatic puncture and drainage can be performed by placing the guide wire into the dilated biliary duct and stent between the duodenum and biliary duct to relieve obstructive jaundice.

EUS-Guided Puncture and Drainage of Pancreatic Cyst

EUS is clinically significant the diagnosis and treatment of pancreatic pseudocyst. EUS-guided puncture of pancreatic pseudocyst can help differentiate pancreatic pseudocyst from cystic tumors and in addition fluid examination help rule out infection. Under the EUS guidance an appropriate location is selected so that the puncture needle can bypass blood vessels and be inserted into the cyst; the guide wire is then placed into the cyst and the drainage stent is placed into the cyst through the guide wire.

EUS-Guided Neurolytic Celiac Plexus Neurolysis

EUS-guided celiac plexus neurolysis is intended for treating severe abdominal pain caused by conditions such as pancreatic cancer, chronic pancreatitis, etc. by injecting drugs at the region of celiac ganglion with a linear array ultrasonic endoscope. Guided by EUS, local anesthetics, neurolytic agent or corticosteroids are injected to the region of celiac ganglion to relieve pain by blocking and destroying the nerve plexus.

The endoscopic ultrasonography-guided fine needle injection (EUS FNI) can be used for EUS-guided cholangiopancreatography, celiac plexus neurolysis, injection of botulinum toxin and also local injection in tumors. The EUS guidance not only provides accurate location but facilitates short puncture pathways, reducing side injuries and complications due to the leakage of drugs. Doppler featured EUS helps image the blood vessels to prevent vascular damage.

The EUS-guided radiofrequency ablation is intended for treating advanced tumor by penetrating into tumor tissues with a radiofrequency generator guided by EUS and necrosing tumor tissues by means of radiofrequency ablation.

EUS-Guided Radioactive Particle Implantation

Under the EUS guidance, a puncture needle with radioactive particles is inserted into pancreatic tumor tissues and then internal irradiation is employed to destroy the tumor tissues.

1.2 Narrow Band Imaging

1.2.1 Introduction

With the improvement of endoscopic technology and wide use of chromoendoscopy and magnifying endoscopy, most digestive tract lesions can be detected at early stage. The new endoscopic technologies, narrow band imaging (NBI- Olympus), i-Scan (Pentax) and FICE (Fujinon) enabled increase detection of mucosal lesions of the digestive tract. Our experience is with NBI.

NBI is a high resolution technique by using a special filter that converts white light into blue, green and red lights with wavelengths 485–515 nm, 430–460 nm and 400–430 nm respectively (Fig. 1.5). Blue light penetrates superficially, whereas red light penetrates to deeper mucosal layers. Images formed by these three lights are displayed on a monitoring device after being integrated by the image adjustment circuit of the endoscopic system to enhance the fine structure of the mucosal surface, morphology of capillaries without the use of chromoendoscopy. Clinically, NBI is used in combination with magnifying endoscopy to better observe the mucosal and vascular patterns of the lesions.

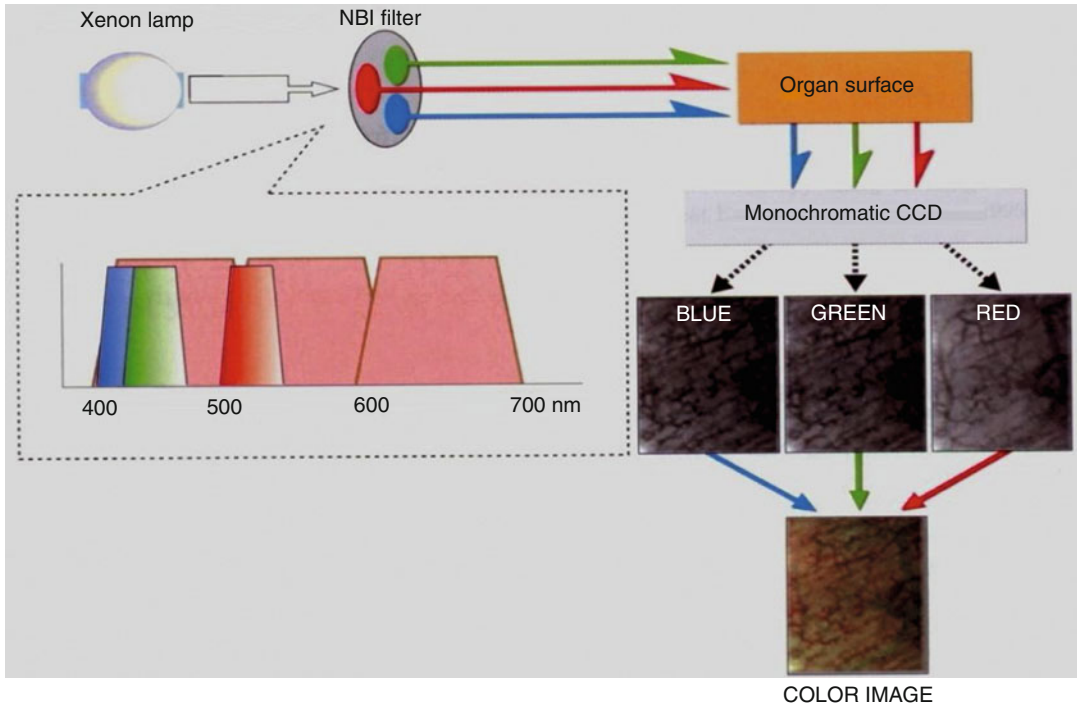

Fig. 1.5 Imaging principle of NBI technology. Narrow the bandwidth through the optical filter, with wavelength ranging at 415, 455 and 500 nm (Courtesy of Olympus China)

1.2.1.1 Gross Morphology Classification

In digestive lesions the widely used morphology classification is Paris classification (Fig. 1.6).

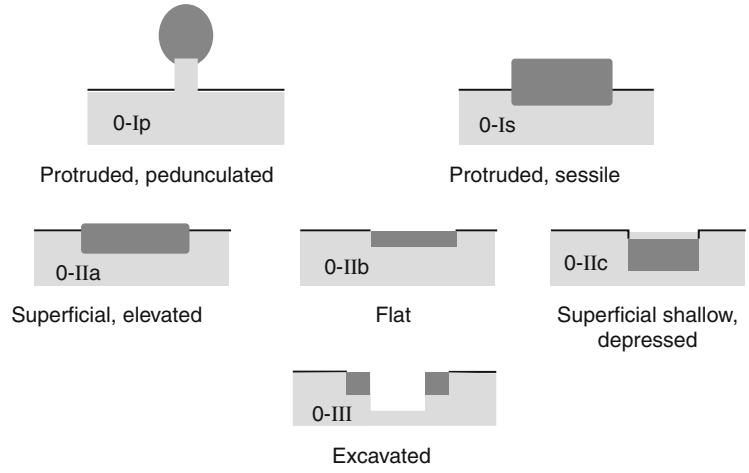

Fig. 1.6 Paris classification of type 0 neoplastic lesions of digestive tract (With permission from *Gastrointestinal endoscopy* [5])

1.2.2 Application of NBI in Diagnosis of Barrett's Esophagus

The incidence of adenocarcinoma in patients with Barrett's esophagus is about 0.5 percent per year and the prognosis is poor. A periodic upper GI endoscopy with biopsy is often used to monitor people with Barrett's esophagus and watch for signs of cancer development. Dysplasia occurs in Barrett's tissue. Dysplasia is precancerous and is classified as low grade or high grade that can lead to esophageal cancer.

Therefore, in making a diagnosis of Barrett's esophagus two aspects need to be covered: one is to detect the extent and the other is to detect intestinal metaplasia and the area where atypical dysplasia may be present (Fig. 1.7). Compared to conventional endoscopy, NBI clearly makes the distinction between the Barrett and normal esophageal mucosa. In combination with magnifying endoscopy, the mucosal and vascular patterns can be observed which helps identify the intestinal metaplasia and dysplastic area for targeted biopsy, thus increase diagnostic yield.

Compared to conventional endoscopy, NBI is more advantageous in diagnosis and follow-up of Barrett's esophagus. NBI clearly visualize the boundary between the gastric mucosa and esophageal mucosa by chromatic contrast, which facilitates the detection of the lesions of Barrett's esophagus. In Barrett's esophagus, it is difficult for conventional endoscopy to accurately differentiate high-grade intraepithelial neoplasia (HGIN) from specialized intestinal metaplasia (SIM). In Contrast, NBI in combination with magnifying endoscopy enhances mucosal structure and vascular pattern within the suspected area and can help evaluate and differentiate between HGIN and SIM. Flat mucosa (without villi or pits) with regular mucosal and vascular pattern is associated with SIM, whilst irregular mucosal and vascular pattern or abnormal blood vessels are suggestive of HGIN. A prospective study found NBI detected more patients with dysplasia and HGIN with fewer biopsies when compared with standard endoscopy.

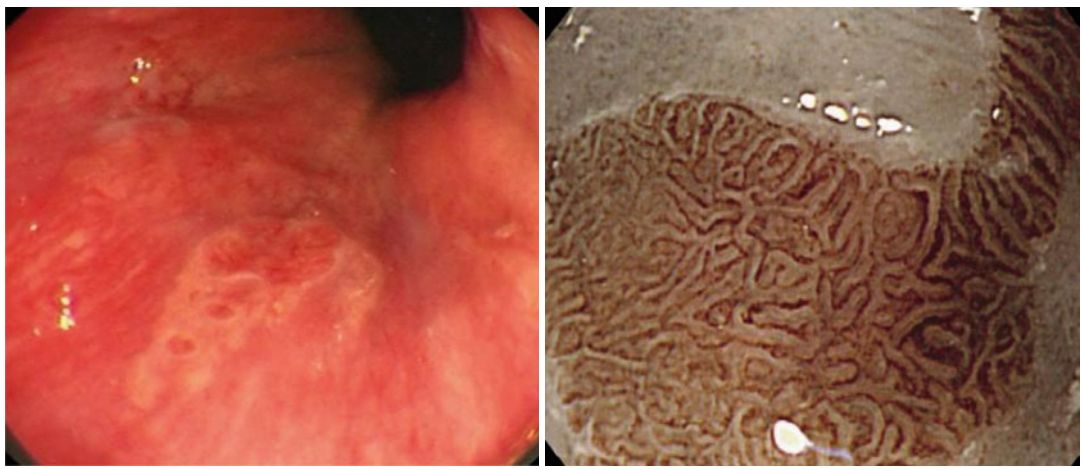

Fig. 1.7 NBI defines the boundary between Barrett's mucosa and normal squamous epithelium

1.2.3 Application of NBI in Diagnosis of Early Esophageal Cancer

The morbidity and mortality of esophageal cancer remains high and the overall 5-year survival rate is lower than 10 %, because most patients diagnosed at late stages in China.

However, overall 5-year survival of early esophageal cancer if treated by ESD is 100 % in patients with HGINs/m2 (i.e. intraepithelial neoplasm or invasive carcinoma limited to the lamina propria mucosa) and 85% in patient with m3/sm (i.e. invasive carcinoma deeper than the lamina propria mucosa) [6]. Thus early detection and treatment of early esophageal cancer is critical to improve long-term survival and outcome.

It is relatively easy to diagnose advanced stage esophageal cancer, but detection of early lesions, particularly flat or small lesions can be difficult and diagnosis is highly dependent on the endoscopist's experiences and expertise. Chromoendoscopy, particularly Lugol staining in esophagus can highlight early esophageal cancer and precancerous lesions but this is time consuming and in addition dye can be irritant to esophageal wall. NBI has a high detection rate of the early esophageal cancer. Clinical studies suggest that NBI can achieve the same result as that by chromoendoscopy without the need of dye. It can detect the lesions and determine the extent of it.

Through NBI, we can see that normal esophageal mucosa is nattier blue, and, by magnification esophageal intraepithelial vessels and deep vessels appear tawny and cyan (Fig. 1.8).

Observation of intra-epithelial papillary capillary loops (IPCL) with NBI combined with magnifying endoscopy help detect early esophageal cancer. Clinically, IPCLs are classified into the following types: a. Type IPCL-I, short and fine with scattered distribution and usually seen in the superior segment of normal esophagus; b. Type IPCL-II, long and thick, distributed more densely than the superior esophagus and usually seen in the middle segment of normal esophagus; c. Type IPCL-III, in which IPCL tip splits and expands and IPCL is dense and evenly distributed, usually seen in the inferior segment of normal esophagus; d. Type IPCL-IV, flexioned; e. Type IPCL V-1, in which IPCL splits and expands with different calibers, morphologies and uneven distribution; Type IPCL V-2, the extension of IPCL V-1; Type IPCL V-3, where IPCL is highly destructed with the tilting vessels extended; Type IPCL-VN, where IPCL is destructed with morphologically different and disorderly running new tumor vessels generated (Fig. 1.9).

The IPCL change pattern is closely related to the depth of lesion infiltration and different IPCLs reflect different depths of infiltration. Type IPCL IV and V-1 can be observed in dysplasia and m1 cancer, Type IPCL V-2 can be observed in m2 cancer, Type IPCL V-3 can be observed in m3 and sm1 cancers and Type IPCL VN can be observed in below sm2 cancer and progressive cancer. NBI combined with magnifying endoscopy can accurately determine the depth of infiltration by esophageal cancer to provide accurate basis for the selection of treatment options for early esophageal cancer and this seems the main advantage of NBI over chromoendoscopy (Fig. 1.9) [7].

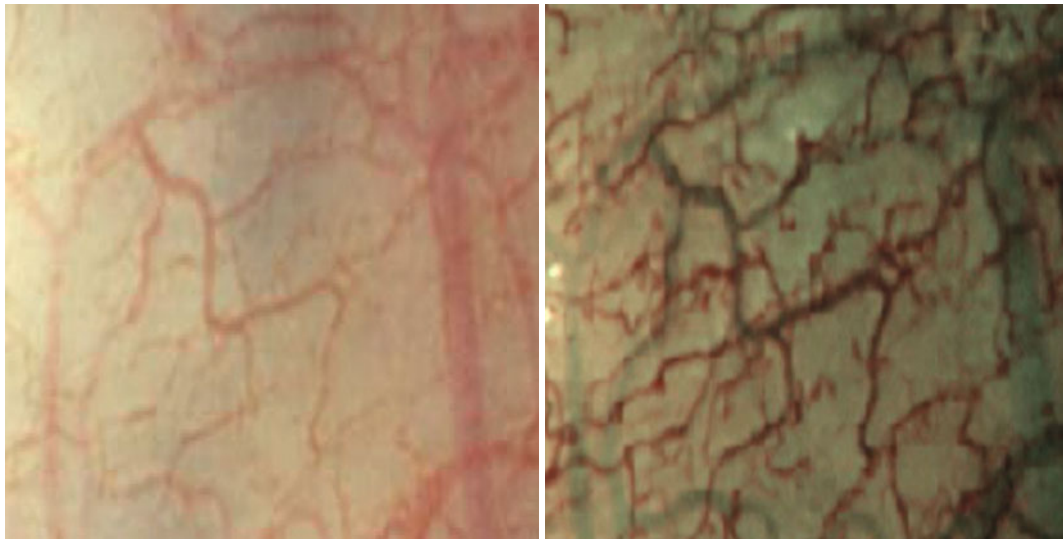

Fig. 1.8 NBI Magnifying endoscopy shows the superficial vessels are tawny and those in deep layers are cyan

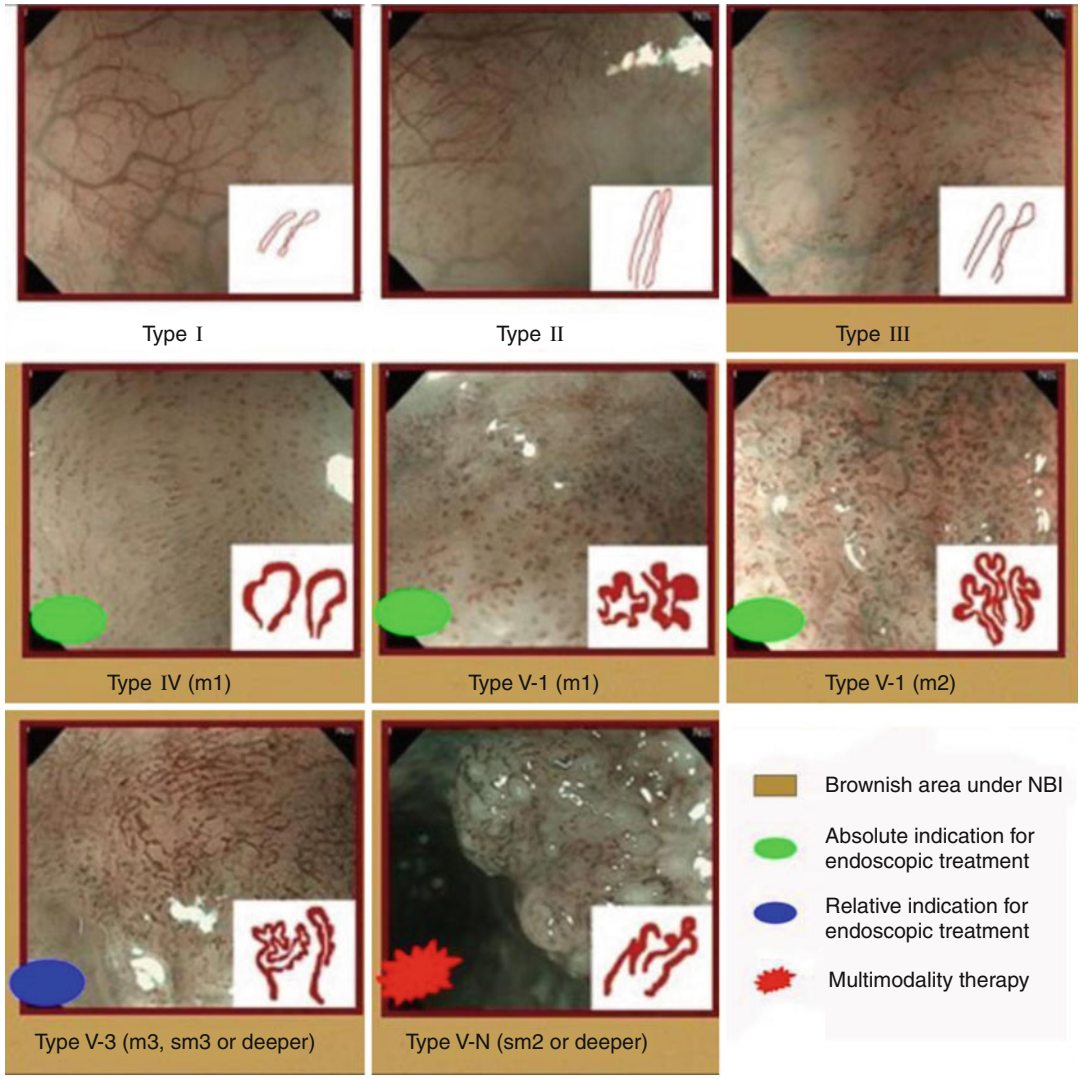

Fig. 1.9 IPCL pattern classification (Reprinted from Chai et al. [8])

1.2.4 Application of NBI in Diagnosis of Early Gastric Cancer and Ampullary Cancer

NBI also plays an important role in the diagnosis of early gastric cancer. Magnifying endoscopy combined with NBI can better visualize mucosal pattern and microvascular pattern that helps diagnose early gastric cancer (Fig. 1.10). Nakayoshi et al. reported prediction of the histological type of the lesions by observing the structure of the mucosal surface and structure of the capillaries on such surface of the early gastric cancer lesions [9].

Uchiyama et al. reported early ampullary tumors by combing NBI with magnifying endoscopy to observed Pit pattern of the lesions and the structure of local capillaries to differentiate the nature of the lesions and determine suspected areas for the purpose of targeted biopsy thus increasing the positive rate of the biopsy (Fig. 1.11) [10].

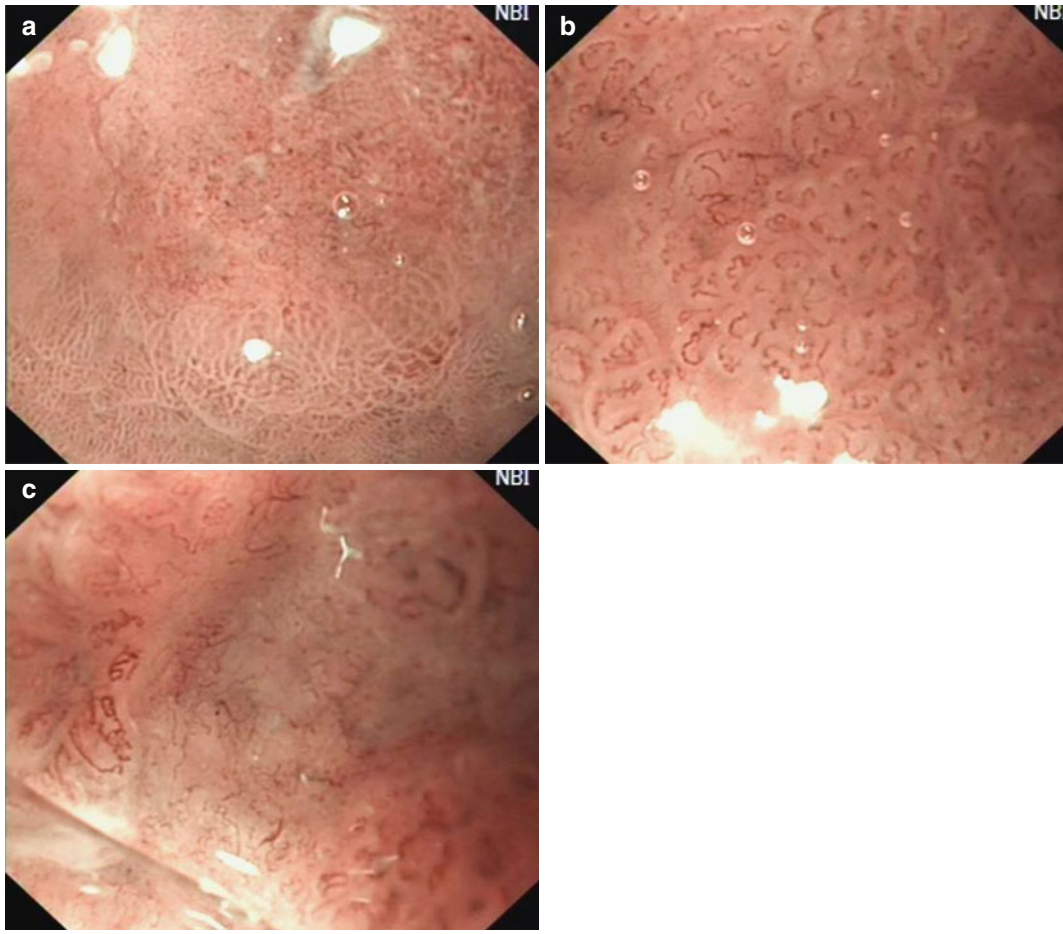

Fig. 1.10 Images of early gastric cancer observed by NBI combined with magnifying endoscopy. (**a**) Lesions are more demarcated on NBI view; (**b**) Vascular disturbance on the mucosal surface; (**c**) Tumor associated angiogenesis

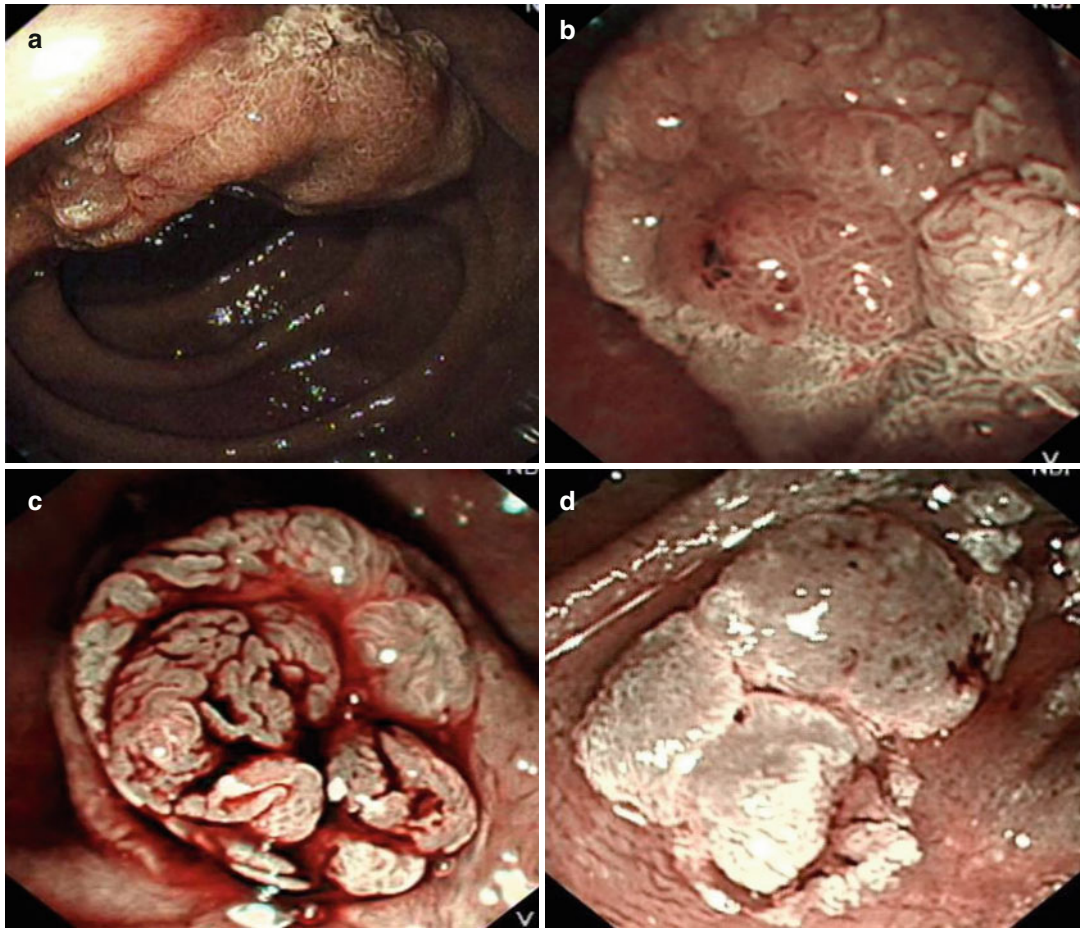

Fig. 1.11 Images of descending duodenal lesions observed by NBI. (**a**) A polyp around the duodenal papilla; (**b**) Tumor of duodenal papilla; (**c**, **d**) Recurrent tumor of papilla after previous EMR

1.2.5 Application of NBI in Diagnosis of Colorectal Mucosal Lesions

Despite ongoing technological progress, colonoscopy still has a substantial miss rate for colon polyps and flat lesions that may lead to colorectal cancer even in patients undergoing endoscopic surveillance. Excellent bowel preparation and appropriate withdrawal time (>6 min) has shown to increase polyp detection rate.

Recently studies confirmed that chromoendoscopy can detect more polyps than a standard colonoscopy. It takes longer to perform than a standard colonoscopy and requires additional kit such as spraying catheter and special blue dye.

Narrow-band imaging (NBI) is an optical image enhancement technology that enhances vessels and their patterns in the mucosa hence can be helpful in differentiating tumorous from non-tumorous lesions.

Examination of the lower digestive tract with NBI can visualize capillaries on the mucosal surface that appear as brown. Capillary network images are superior to conventional colonoscopy (Fig. 1.12).

Due to the difference between capillaries pattern of mucosal lesions and adjacent normal in density, morphology and color, NBI can clearly visualize the demarcation and surface structure of the lesions (Fig. 1.13).

In the NBI mode, it is possible to observe the fine structure of the superficial mucosal layer and distribution of capillaries. As capillaries on the normal superficial mucosal layer around the colonic tumorous lesion extend until they reach the lesion margin and this enables the demarcation between the tumorous lesions and normal adjacent mucosa to be clear. Moreover, by narrow-band lights the lesions is shown in deeper color that is highlighted more clearly due to the denser distribution and structural disturbance of the vessels within the tumorous lesions.

To evaluate morphology, magnifying endoscopy with indigo carmine or methylene blue can be used to observe the pit pattern of the polyp and to determine the nature of it in real time. NBI works similarly as chromoendoscopy (Fig. 1.14) by obtaining high-resolution images equivalent to chromoendoscopy while the latter can not observe the vascular pattern. Some scholars believe that the pit pattern classification of neoplasia by NBI combined with magnifying endoscopy is more reliable and such procedure is described as “optical biopsy” [11].

The well recognized morphology classification is Kudo’s Pit Pattern [12] (Fig. 1.15) and capillary pattern (CP) classification proposed by Sano [13] (Fig. 1.16).

Kudo’s pit pattern type I is normal mucosa. Type II includes stellar or papillary pits, and these pits always indicate hyperplasia (Fig. 1.17). Type IIIs includes small tubular or round pit that are smaller than normal pits, and they indicate adenoma in 73 % or intramucosal adenocarcinoma in 28 % of these lesions. Such lesion are amenable endoscopic resection. Type IIIL includes tubular or roundish pits that are larger than normal pits. Almost all of Type IIIL lesions are tubular adenomas in pathology, which can be treated by polypectomy. Type IV includes branch-like or gyrus-like pits, most of which are tubulovillous adenoma, although intramucoal carcinoma is present in 35 % of these pits and can be treated by endoscopy (Fig. 1.18). Type VI includes irregularly arranged pits that may indicate submucosal invasive carcinoma in majority of such lesions, for which the optimal treatment can be decided between endoscopic and surgical therapy (Fig. 1.19). Lastly, type VN includes nano structured pits, which indicate massive submucosal invasive carcinoma and require surgical resection with lymph node dissection [14].

(4) CP types I, II, IIIA, and IIIB are observed in non-neoplastic lesions, adenomas, mucosal or slightly invasive submucosal carcinoma, and massive invasive submucosal carcinoma, respectively Fig. 1.20. The reported accuracy for distinguishing low-grade dysplasia from high-grade dysplasia/invasive cancer was 95.5 % and sensitivity of 90.3 % [16]. Thus Capillary patterns observed by NBI with magnification could be used to assess the degree of atypia in early colorectal neoplasia.

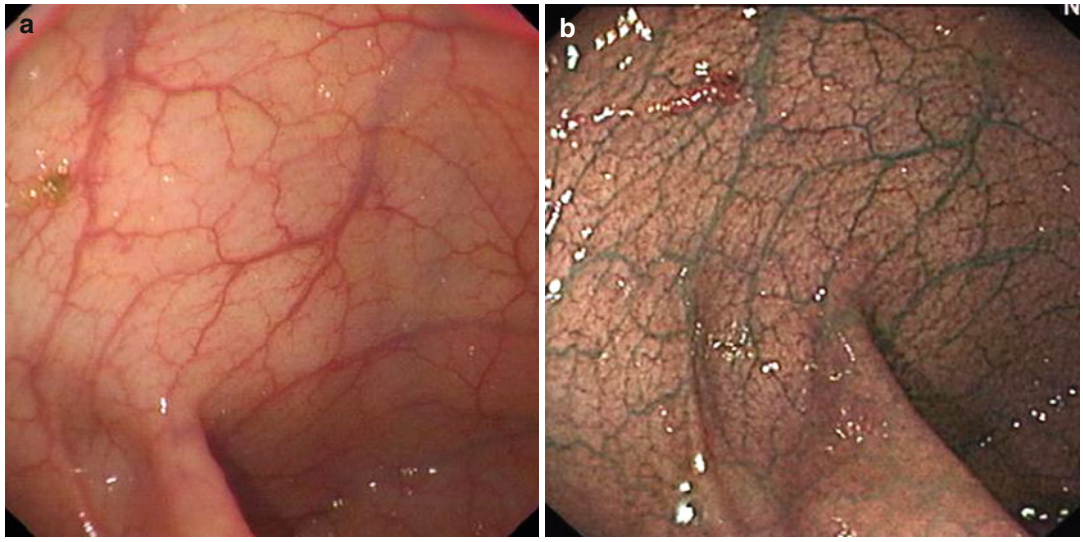

Fig. 1.12 Comparison of colorectal capillary network images obtained by conventional colonoscopy and NBI. (**a**) The mucosal vein and capillaries are visible; (**b**) The mucosal vein and finer capillary network can be clearly observed by NBI

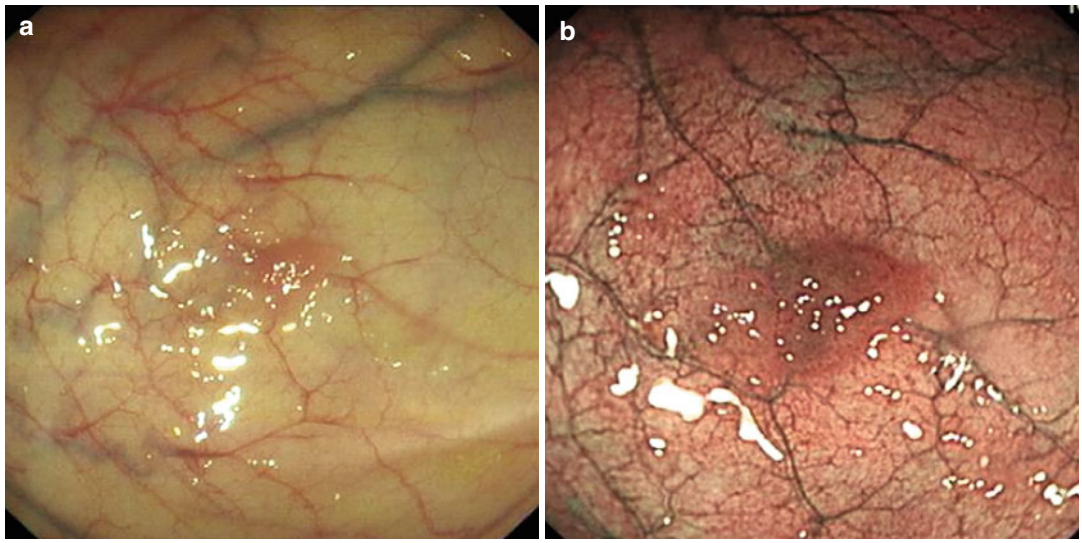

Fig. 1.13 Comparison between colorectal lesions and adjacent normal mucosa images obtained by conventional colonoscopy and NBI. (**a**) Rectal polyp not seen by conventional colonoscopy (IIa); (**b**) Polyp can be clearly seen by NBI

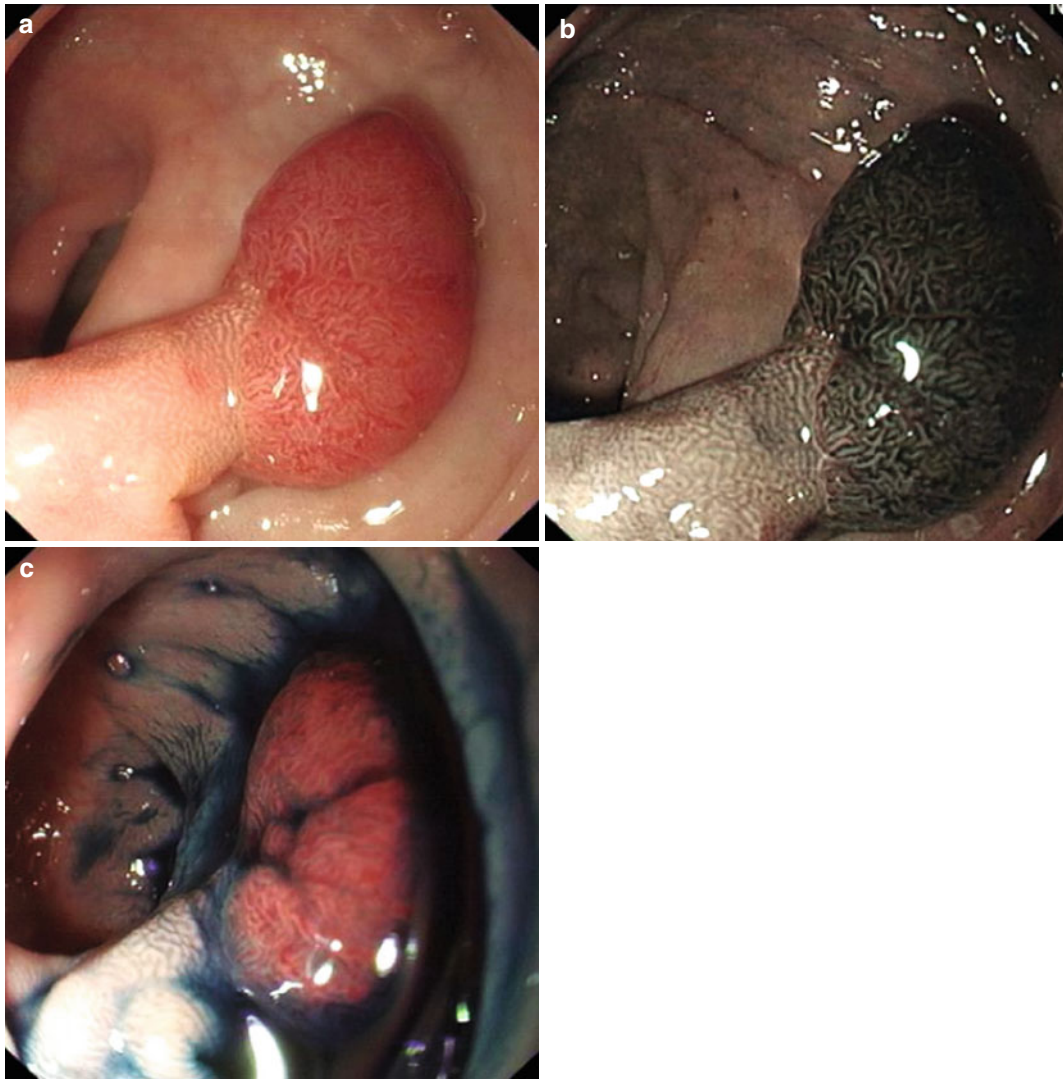

Fig. 1.14 Comparison of a colorectal lesion obtained by conventional colonoscopy, NBI and chromoendoscopy. (**a**) The polyp is in the sigmoid colon (Ip); (**b**) The pit pattern can be clearly observed by NBI; (**c**) After dyeing with indigo carmine

I		Round pid (normal pit)
II		Asteroid pit
IIIs		Tubular or round pit that is smaller than the normal pit (Type I)
IIIL		Tubular or round pit that is larger than the normal pit (Type I)
IV		Dendritic or gyrus-like pit
VI		Irregular arrangement and sizes of IIIL, IIIs, IV type pit pattern
VN		Loss or decrease of pits with an amorphous structure

Fig. 1.15 Kudo's pit pattern classification (With permission from Tanaka et al. [14])

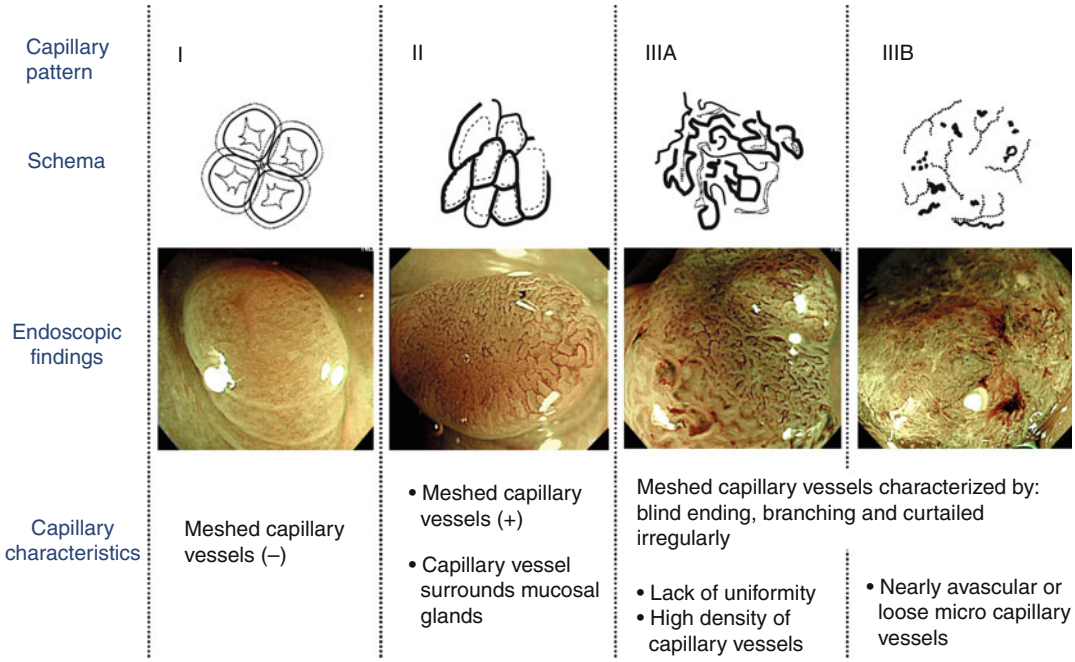

Fig. 1.16 Classification of capillary pattern by magnified NBI (Reproduced from Ikematsu et al. [15])

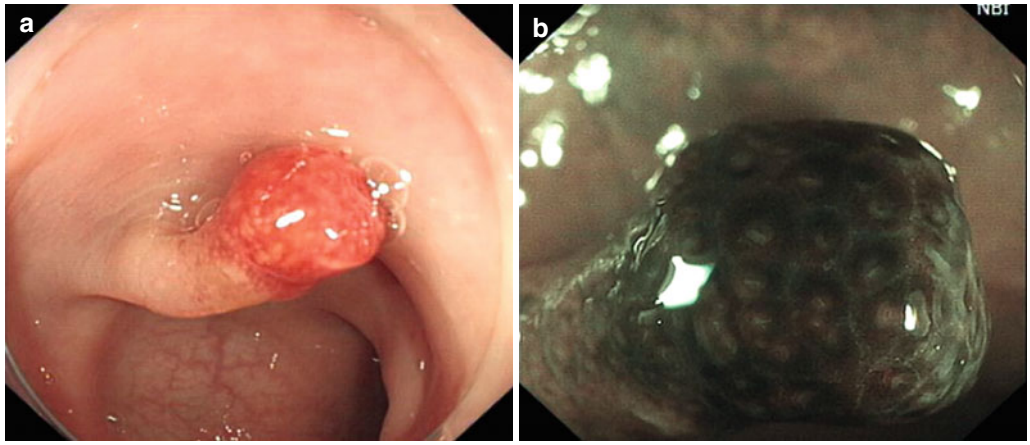

Fig. 1.17 Ip colonic lesion (**a**) with type II pit pattern (**b**)

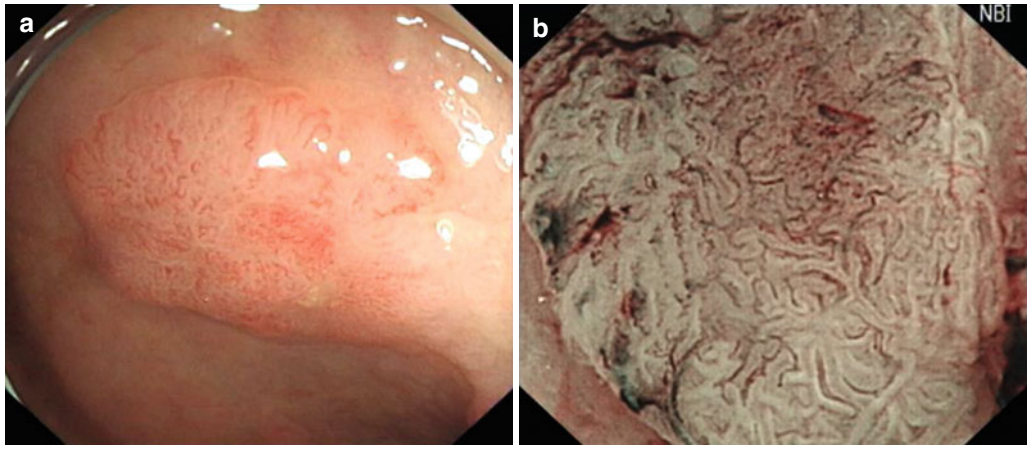

Fig. 1.18 IIa colonic lesion (**a**) with type IV pit pattern (**b**)

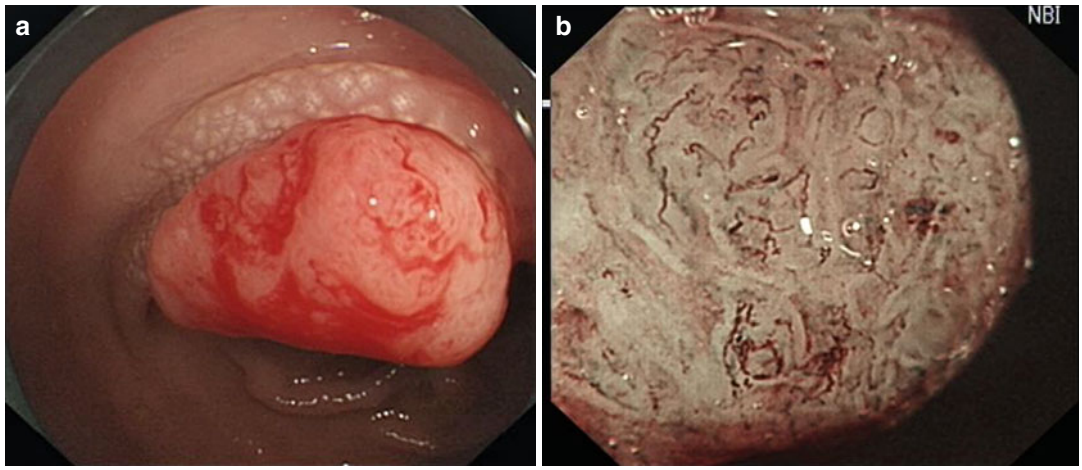

Fig. 1.19 Colonic lesion (**a**) with type VI pit pattern (**b**)

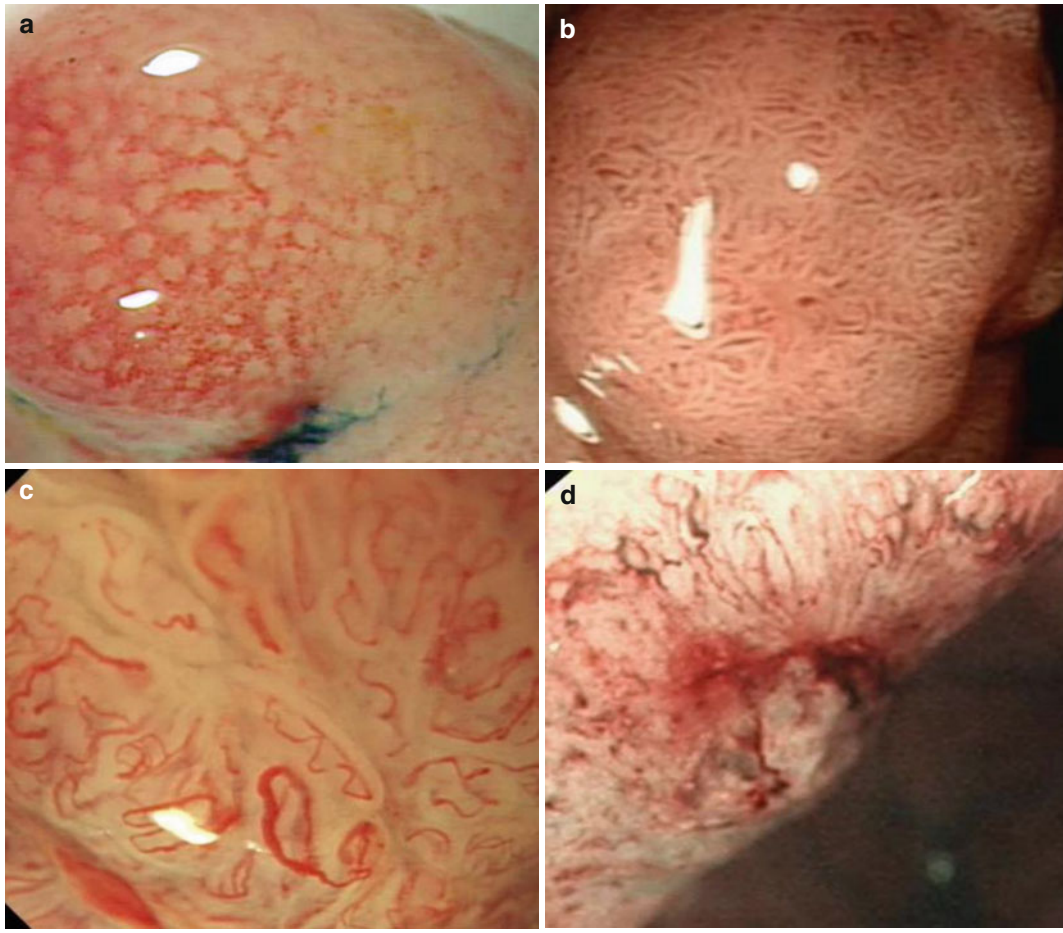

Fig. 1.20 Capillary pattern of colorectal polyp on NBI. (**a**) No meshed capillary vessels can be seen (type I); (**b**) There are meshed capillary vessels surrounding the mucosal glands (type II); (**c**) Irregular meshed capillary vessels (type IIIA); (**d**) Irregular meshed capillary vessels nearly invascular or loose microcapillary vessels (type IIIB)

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