

Application of 3D visualization and 3D printing technology on ERCP for patients with hilar cholangiocarcinoma

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Abstract. Endoscopic retrograde cholangiopancreatography (ERCP) is an important treatment for inoperable hilar cholangiocarcinoma (HCC). The aim of the present study was to evaluate the clinical value of three-dimensional visualization (3DV) and 3D printing (3DP) technologies for ERCP in patients with HCC. The clinical data of 15 patients with HCC admitted for ERCP were analyzed retrospectively, including 9 males and 6 females. Thin-sliced data of computed tomography and magnetic resonance cholangiopancreatography (MRCP) were acquired and imported into Mimics Innovation Suite v17.0 software for 3D reconstruction. Standard Template Library files were exported for 3D printing. The target bile duct and Bismuth-Corlette (BC) classification were selected and performed respectively with the aid of Mimics Innovation Suite v17.0 software. The results were compared with the selected ones in ERCP. 3DV and 3DP models were successfully constructed for all patients, which presented the tumor, bile duct and the spatial relationship between them from multiple perspectives. The ERCP of all patients in the present study were performed successfully. The target bile duct screened by them had a high concordance rate of 86.7% with that in ERCP. The diagnostic accuracy of BC type results by 3DV and 3DP models was 93.3%. 3DV and 3DP technologies can accurately show the tumor and its associations with the surrounding bile duct, and it can be used to guide ERCP in HCC patients and improve the success rate of the operation.

Introduction

Cholangiocarcinoma is a malignant neoplasm that originates from the epithelium of the biliary tree (1). Hilar cholangiocarcinoma (HCC) is the most common type of cholangiocarcinoma, accounting for about 50-60% (2,3). HCC arises from the right and left hepatic ducts, the confluence of the right and left hepatic bile ducts, and above cystic duct openings. At present, surgical resection is still the only effective way to cure HCC (4). However, because of its location, prone to local invasion, adjacent structure infiltration and metastatisation, surgical operation is very difficult and quite often not radical. In addition, presenting with insidious onset and lacking specific symptoms, most patients are diagnosed in advanced stage and lost the opportunity of surgical treatment. Consequently, the radical (R0) resection rate is only 10-20% (5). The survival rates of five years after complete surgery range from 11 to 41% (6). So as a safe and effective palliative therapy, the biliary stent placed by endoscopic retrograde cholangiopancreatography (ERCP) may be the best choice for patients with unresectable HCC (7). However, violated by the tumor, the left and right hepatic bile ducts are not communicating with each other, which leads to the difficulty of superselective catheterization and the failure of ERCP. Correct and reasonable selection of the target bile duct is the key to superselective catheterization of bile duct successfully. At present, the choice of target bile duct is mainly based on preoperative CT, magnetic resonance cholangiopancreatography (MRCP) and intraoperative cholangiography. But for complex HCC, it is difficult to determine the target bile duct. So the ERCP is still full of challenge.

Since the early 2000s, three-dimensional printing (3DP) technologies have begun to be applied in medical domain (8). In recent years, the application of 3DP technologies is more and more extensive, such as personalized surgical planning and guidance, medical research and premedical education (8-11). Compared with CT, magnetic resonance imaging (MRI) and other two-dimensional images, three-dimensional visualization (3DV) and 3DP models are more intuitive and more accurate in displaying anatomical and spatial structure of the organs and have made great achievements. Their application value on surgical treatment of HCC has been affirmed (12,13). But the application of 3DV and 3DP technologies on ERCP is still in the early stage and less reported in the literature.

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The objective of this study was to assess the role of ERCP for HCC based on 3DV and 3DP technologies at a center in China.

Materials and methods

Patients. The present study was in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000. The Institutional Ethics Committee of our hospital approved this study, and written informed consent was obtained from each participant before the study. 15 patients with HCC who underwent ERCP were enrolled from January 2015 to January 2017, including 9 males and 6 females. CT and MRCP examination were acquired and 3DV models were constructed. The real three-dimensional models of the tumor and surrounding bile ducts were created by the 3DP technologies. Before the operation, all patients were informed of the indication and details of ERCP and the risks and complications of the operation.

Instruments. CT: The data of 1 mm slice thickness were acquired from the 64-MDCT provided by American GE Company. MRCP: The 1.5 T Signa HDxt provided by GE Healthcare Bio-Sciences (Pittsburgh, PA, USA) was utilized to obtain the 1.8 mm slice thickness.

3DV and 3DP technologies. Data of CT and MRCP were imported into 3D visualization workstation that called Mimics Innovation Suite v17.0 software in DICOM format, where 3DV models of liver tumor and bile ducts were reconstructed. The reconstructed models were exported as Standard Template Library files. The topological correction, decimation, Laplacian smoothing, and local smoothing were needed to create a 3D model for 3DP. ProJet® 4500 3D printer (3D Systems Corp., Circle Rock Hill, SC, USA) was used to manufacture the models and the printing material was Visijet C4 Spectrum Core. Bismuth-Corlette (BC) type was performed and diameter of the dilated bile ducts was calculated. The bile duct with the largest diameter and the widest drainage area was selected as the target bile duct and compared with the actually selected ones in ERCP.

ERCP. Now it is still controversial whether unilateral or bilateral drainage is better in the treatment of HCC. Unilateral stenting appears to be adequate for relieving jaundice in most unresectable cases. And it is technically easier and less expensive than bilateral stenting, with reintervention for stent dysfunction also being considerably easier (14). At the same time, in consideration of the tolerance of surgery and postoperative complications, so unilateral stenting was performed for all patients in our study. At first, the drainage area and target bile duct were selected preliminarily on the basis of preoperative abdominal CT, MRCP image and intraoperative cholangiography. The bile duct was selectively cannulated using a guide wire. If encountered difficulties, the sphincterotomy was performed. The bile was extracted by a syringe after successful selective intrahepatic bile duct cannulation as much as possible to lower the pressure of the bile duct. The dilating bougie was used to dilate the stenosis along the

guide wire. According to the patients' medical history, BC type, patients and their families' wishes, the biliary stents were chosen rationally. Finally, the metal or plastic stent was placed successfully and nasobiliary duct was inserted and fixed smoothly.

Results

3DV models were successfully manufactured for all patients that clearly displayed all the relevant structures, including intrahepatic bile ducts; size, shape, location of the tumor; anatomical structure between them; location and degree of the biliary stricture. Moreover, 3DV models could be amplified, rotated, and hyalinized to clarify the anatomic character of these structures with omnidirectional, multiple-angle, and multilevel views. The models can localize correctly the tumor and surrounding bile ducts, identify the extent of biliary stenosis and cholangiectasis, contribute to determining the target bile duct and make target bile duct be selected intuitively, concretely and objectively. The location and direction of target bile duct can be used to direct selective intrahepatic bile duct cannulation in ERCP. Furthermore, 3DV models can avoid the influence of subjective factors such as the operator's own experience, the level of imaging ability to ERCP, and the success rate is higher. Demographics and research variables are shown in the Table I. The target bile duct screened by the models had a high concordance rate of 86.7% with that in ERCP. The results were different in two patients. The target bile duct identified by 3DV and 3DP models was the right posterior lobe bile duct. However, selective cannulation of the right posterior lobe bile duct failed, we had to try the left lateral lobe bile duct and succeed. The diagnostic accuracy of BC type results by 3DV and 3DP models was 93.3%.

ERCP was performed successfully for all patients. After ERCP, the malignant obstructive jaundice symptoms of 13 patients were alleviated or disappeared. Preoperative and postoperative laboratory features including white blood cell (WBC), neutrophil ratio (Neu%), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL) and direct bilirubin (DBIL), are shown in Table II. The TBIL level of 2 cases did not decrease, or even increased. BC type for the two patients was both Type IV and the cancer metastasize to the liver and portal vein. Besides, cholangitis was induced by ERCP. So their prognosis was poor, just like the findings of Vienne and his colleagues. They thought complete resolution of jaundice might not occur for patients with Bismuth IV after ERCP because it was now thought that at least 50% of normal liver needs to be drained to achieve complete resolution of jaundice (15). The change of TBIL for all patients before and 3 days after operation was listed in Fig. 1. Cholangitis, postoperative pancreatitis and hyperamylasemia occurred in 2, 1 and 4 cases respectively. And the patients were discharged in 6-20 days. All patients were followed up for three months to one year and three cases were died.

The specific diagnosis and treatment process of a typical case were reported as follows: A 75-year-old male was admitted for yellow skin and mucosa for one week. And he had a medical history of hepatitis B cirrhosis. CT scan and MRCP showed a mass in hepatic portal and dilatation of intrahepatic

Table I. Demographics and research variables.

Variable	No. of patients (n=15)
Female/Male	6/9
Age, years	65.4±14.9
BC type (II/IIIA/IIIB/IV)	
Model	2/4/4/5
ERCP	2/5/4/4
Concordance rate	14/15 (93.3%)
Target bile duct	
Model	R, R, L, L, R, R, L, R, R, R, L, R, R, L, L
ERCP	R, R, L, L, L, R, L, R, R, L, L, R, R, L, L
Concordance rate	13/15 (86.7%)

R, right posterior lobe bile duct; L, left lateral lobe bile duct; ERCP, endoscopic retrograde cholangiopancreatography; BC, Bismuth-Corlette.

Table II. Preoperative and postoperative laboratory features.

Variable	Preoperative	Postoperative day 1	Postoperative day 3
WBC	5.8±2.0	9.8±2.0	7.1±2.8
Neu%	71.0±11.6	82.5±10.7	77.6±9.6
ALT	156.1±148.3	92.6±89.1	81.3±91.2
AST	135.3±96.5	95.3±51.1	78.6±82.5
TBIL	237.5±97.6	226.6±102.8	186.2±112.7
DBIL	196.6±82.0	194.1±88.8	158.0±104.6

WBC, white blood cell; Neu, neutrophil ratio; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; DBIL, direct bilirubin.

bile ducts, and the BC type was type II (Fig. 2); The 3DV and 3DP model were constructed successfully and the BC type was type II (Fig. 3). However, in this model of the patient, because of severe dilatation, most of the left bile ducts fused together. But some bile ducts can still be distinguished. The diameters of the dilated bile ducts were calculated by Mimics Innovation Suite v17.0 software (Materialise, Leuven, Belgium). The method was averaging the testing values of repeated measurements. The left and right hepatic bile ducts were marked with different colors and corresponding sequence numbers (Fig. 4A). The diameters of hepatic bile ducts were as follows (Table III).

The final right target bile duct was the right brown bile duct and the corresponding serial number was ①, namely, the right posterior branch bile duct. And the final left target bile duct was ②, namely the left lateral branch. In ERCP, the bile duct of the right lobe (Fig. 4B) was the actual selected bile duct. The double-wire guided technique was applied. Along the guide wire, the nasobiliary duct was placed to the right lobe of the liver. The 3DV model was consistent with intraoperative condition in ERCP, and the selected bile duct was the same. After operation, the patient's symptoms were significantly relieved

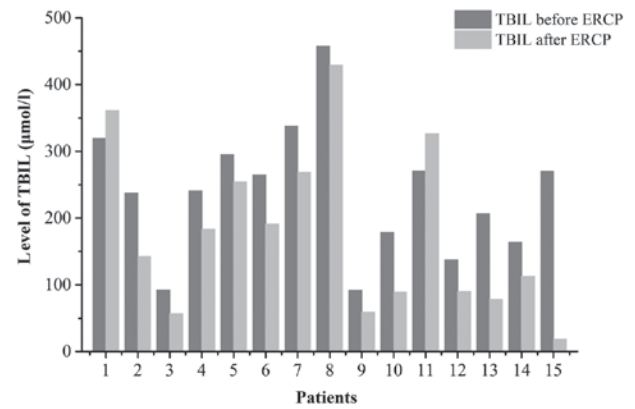


Figure 1. Change in TBIL for all patients prior to and 3 days following their operation. TBIL, total bilirubin.

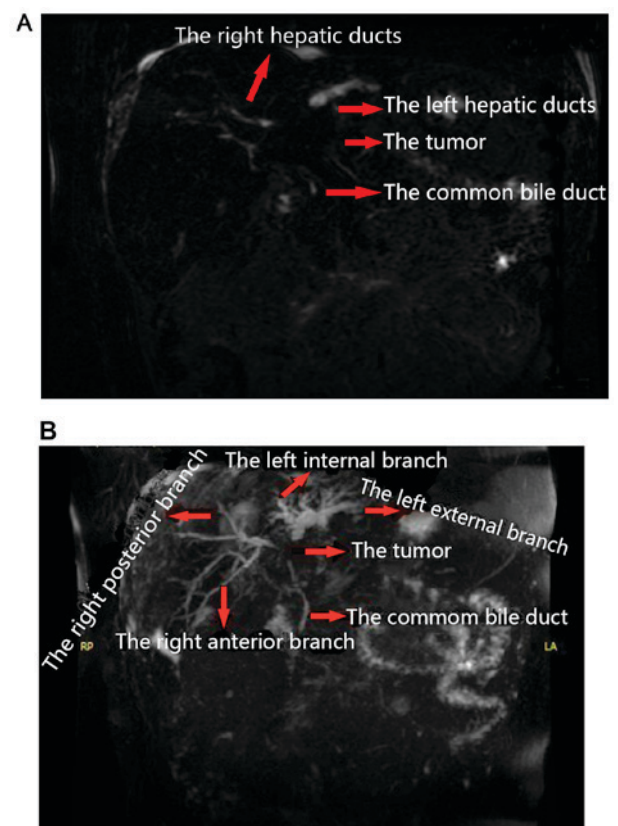


Figure 2. MRCP image of hilar cholangiocarcinoma (male patient, aged 75): Hepatic hilar mass and intrahepatic bile duct dilatation. (A) Two-dimensional image of MRCP. (B) The image of MRCP three-dimensional reconstruction. MRCP, magnetic resonance cholangiopancreatography.

without complications and he was discharged on postoperative day 14, without any complications.

Discussion

HCC is a malignant tumour with high mortality. BC type can accurately delineate the anatomic location of tumor and the degree of invasion and is the most widely used preoperative reference system for predicting resectability and defining surgical strategy. And it also contributes to choose reasonable drainage way in endoscopic therapy and evaluating therapeutic effect.

Table III. Diameter of bile ducts with different colors and the corresponding sequence numbers.

A, Right hepatic duct system

No.	Color	Diameter of bile duct (mm)
1	Brown	7.28 (8.45+5.95+6.74+7.97/4)
2	Yellow	5.68 (6.09+5.49+5.44+5.69/4)
3	Blue	3.77 (4.06+3.30+4.40+3.37/4)
4	Light blue	3.72 (3.00+4.49+3.74+3.65/4)
5	Lilac	6.77 (7.56+6.31+7.01+6.19/4)
6	Pink	4.78 (4.93+4.47+4.50+5.24/4)

B, Left hepatic duct system

No.	Color	Diameter of bile duct (mm)
1	Purple	7.01 (7.74+5.91+8.12+6.27/4)
2	Green	9.12 (8.59+9.54+10.2+8.1/4)
3	Green	13.57 (15.54+12.61+13.52+16.4/4)
4	Green	12.00 (12.78+11.52+10.8+12.72/4)

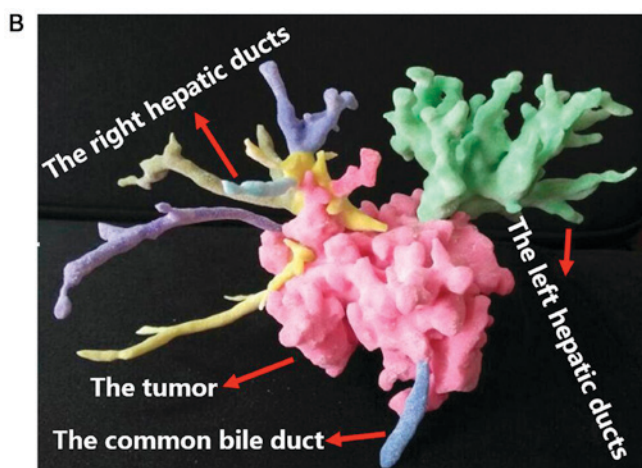
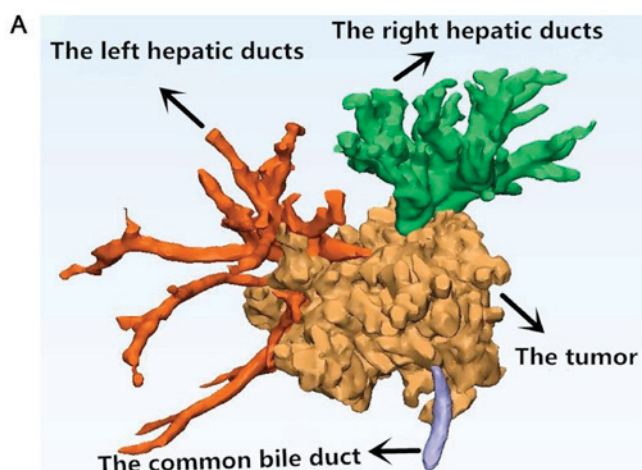


Figure 3. 3DV and 3DP models. (A) The 3DV model generated by MIMICS v17.0 software of the hepatic bile duct system and the mass, including the tumor, the dilated bile duct and the 3D anatomical association between them. (B) The 3DP model presented the tumor and the entire bile duct tree. 3DV, three-dimensional visualization; 3DP, three-dimensional printing.

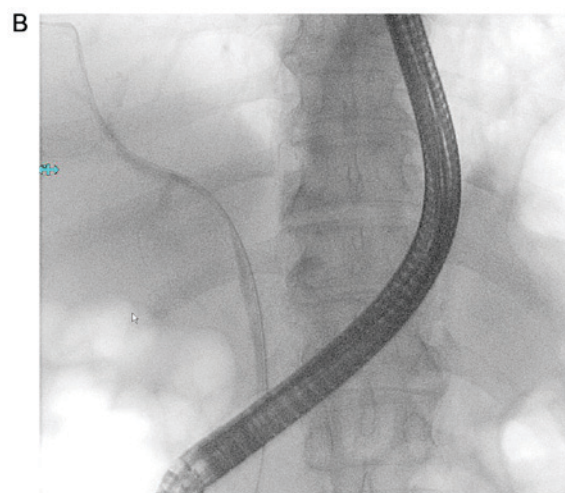
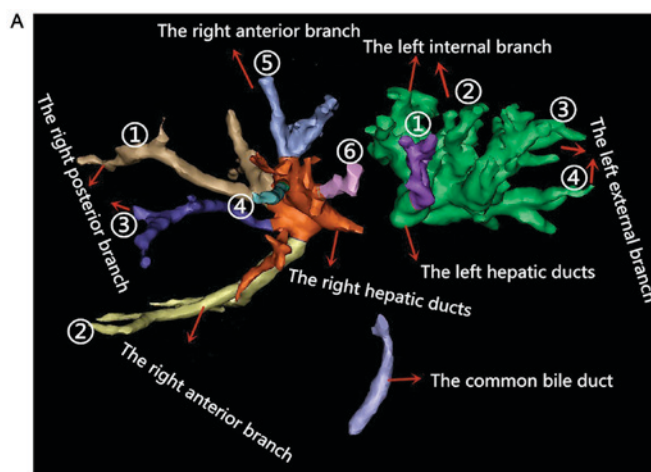


Figure 4. Bile ducts in 3DV model and the image of ERCP. (A) The liver bile duct system without the tumor and the bile ducts identified by different colors. In the right bile ducts, 1 and 3 belong to the right posterior branch, and 2 and 4-6 belong to the right anterior branch. In the left bile ducts, 1 and 2 belong to the left internal branch, and 3-5 belong to the left external branch. (B) The guide wire was inserted into the right hepatic duct in ERCP operation. 3DV, three-dimensional visualization; ERCP, endoscopic retrograde cholangiopancreatography.

Since proposed by Bismuth and Corlette in 1975 (16), the method is still widely used today. The majority of patients with advanced HCC are inappropriate for surgical resection because of the tumor location in the hepatic hilum and adjacent areas, advanced tumor stage, or comorbidities. Additionally, some people are aged, bad general condition and seem hardly to tolerate surgical operation. Therefore, these patients often have a poor prognosis in terms of survival and quality of life. So as a nonsurgical and palliative treatment, biliary stent placed by ERCP may be the best choice for these people to relieve malignant obstructive jaundice and improve hepatic function, raise living quality and prolong survival time. This kind of treatment corresponds to the normal physiological characteristics. And compared with surgery, it is less invasive and has fewer postoperative complications.

Since 3DV and 3DP technologies are applied to the clinical medicine, they have been widely used in oral and maxillofacial surgery and orthopedics (17-19). 3D visualization and printing can successfully show the anatomic relationship between tissue organs and surrounding structures. 3DV models could

be amplified, rotated, and hyalinized to clarify the anatomic character of tissue and organ structure with omnidirectional, multiple-angle, and multilevel views. And 3DV models can also be employed to accurately calculate the size and volume of a liver tumor, the diameter and length of blood vessels and bile ducts and the residual liver volume. These functions are also of important clinical significance for preoperative planning and guiding the actual surgical operations. However, compared with 3DP models, there is a certain sense of spatial distance in 3DV models. 3DP models are constructed based on 3DV images and can foresee anatomic structure at surgery truly from multiple dimensions before operation. In addition, 3DP models can be brought into the operation room, provide real-time navigation intuitively for key steps in operation and identify and locate key parts quickly. At present, the research and application of these technologies have also made significant achievements in liver surgery, such as liver transplantation, laparoscopic liver resection, hepatectomy for hepatolithiasis, hepatic hydatid disease (20-27). There also are researches on surgical treatment of HCC. Zeng and colleagues (12) applied 3DV and 3DP technologies to the surgery of HCC and found they played an important role in the accurate preoperative diagnosis, the establishment of the operation plan, precise operation in surgery and improvement of the success rate of surgery. With the help of these technologies, Oshiro Y and Ohkohchi N performed successfully left hepatic lobectomy and extrahepatic bile duct resection for a HCC patient (28).

But for the clinical application of 3DV and 3DP techniques for ERCP in patients with HCC, there were no reports and literature of the relevant studies. In our study, we discover that 3DV and 3DP technologies play a significant role in the successful implementation of ERCP in patients with HCC. This article mainly carries on the elaboration from the following three aspects.

The role of 3DV and 3DP technologies in the selection of target bile duct: Correct and reasonable selection of the target bile duct are important to the successful selective intrahepatic bile duct cannulation in ERCP. There are two factors that determine the target bile duct: The dilatation of bile duct is distinct and the drainage range is extensive. In the present study, 15 patients had a high consistency rate of 86.7% on target bile duct selected by the 3DV models and ERCP respectively. Preoperative 3D reconstruction can clearly show the three-dimensional anatomy of the tumor, dilated bile duct and its anatomical relationship with the tumor (Fig. 3) (29,30). With the help of Mimics Innovation Suite v17.0 software (Materialise, Leuven, Belgium), the diameter of the proximal dilated bile ducts could be calculated directly and accurately, and the bile duct with the largest diameter and the most extensive drainage was selected as the target bile duct. The target bile duct is ordinarily selected based on CT, MRCP and intraoperative cholangiography and other two-dimensional images, which can not exhibit the spatial structure of the bile duct, causing the specific direction of the guide wire in superselective catheterization of bile duct is not completely clear, and even a blind insertion. So the success rate of operation is closely related to the operator's experience and the ability of interpreting the images. However, compared to 2D images, 3DV and 3DP models can show the biliary tree more intuitively, the width and direction of target bile duct more clearly, and can rotate by 360 degree and avoid the influence of subjective factors on ERCP.

The role of 3DV and 3DP technologies in guiding the selection and placement of a biliary stent: The location of drainage in patients with HCC can be selected as the left hepatic duct system, the right hepatic duct system or both. The key determinant is the site of the bile duct stricture. BC type is very important for the rational selection of the drainage site and the judgement of curative effect in endoscopic stent placement. Our study discovers that BC classification classified by the 3DV and 3DP models is more accurate, the 3DV and 3DP models can demonstrate the location of bile duct invaded by the tumor more accurately than CT and MRCP and can be used to guide the selection and placement of a biliary stent.

3DV and 3DP technologies can reduce the use of contrast media: Contrast agents are often needed to outline the stricture in ERCP. However, contrast media injection into intrahepatic ducts without adequate drainage easily leads to uncontrolled cholangitis and poor prognosis. The rate of cholangitis after ERCP was 1-5% (31-33). And what's worse, invaded by the tumor, intrahepatic biliary drainage is poor in HCC patients. To decrease the incidence of this complication, some studies have explored the usefulness of CT or MR cholangiography (MRC) prior to stenting (34,35). Once the bile duct tree is delineated by CT or MRC, selective guidewire cannulation and stenting of the targeted bile duct can be accomplished without contrast injection. Compared with CT/MRI, 3DV and 3DP models are more intuitive and more accurate (36). Consequently, they can reduce the use of contrast media. And we can speculate that 3DV and 3DP models can decrease the incidence of cholangitis. But further case control studies are needed to verify the hypothesis.

In conclusion, compared with 2D images, 3DV and 3DP models be amplified, rotated, and hyalinized to clarify the anatomic character of the tumor and its relationship with the surrounding bile ducts with omnidirectional, multiple-angle, and multilevel views. 3DV and 3DP technologies can help to determine the target bile duct, assist in selective cannulation, guide the selection and placement of biliary stent in ERCP, and reduce the use of contrast media. But our findings require further reverification, because the number of cases in this study is too small. More case studies are needed to further validate the conclusion.

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