DOI: 10.1002/jhbp.1091

CONSENSUS STATEMENT

The Tokyo 2020 terminology of liver anatomy and resections: Updates of the Brisbane 2000 system

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The Japanese Society of HBP Surgery

Abstract

Background: The Brisbane 2000 Terminology for Liver Anatomy and Resections, based on Couinaud's segments, did not address how to identify segmental borders and anatomic territories of less than one segment. Smaller anatomic resections including segmentectomies and subsegmentectomies, have not been well defined. The advent of minimally invasive liver resection has enhanced the possibilities of more precise resection due to a magnified view and reduced bleeding, and minimally invasive anatomic liver resection (MIALR) is becoming popular gradually. Therefore, there is a need for updating the Brisbane 2000 system, including anatomic segmentectomy or less. An online "Expert Consensus Meeting: Precision Anatomy for Minimally Invasive HBP Surgery (PAM-HBP Surgery Consensus)" was hosted on February 23, 2021.

Methods: The Steering Committee invited 34 international experts from around the world. The Expert Committee (EC) selected 12 questions and two future research topics in the terminology session. The EC created seven tentative definitions and five recommendations based on the experts' opinions and the literature

review performed by the Research Committee. Two Delphi Rounds finalized those definitions and recommendations.

Results: This paper presents seven definitions and five recommendations regarding anatomic segmentectomy or less. In addition, two future research topics are discussed.

Conclusions: The PAM-HBP Surgery Consensus has presented the Tokyo 2020 Terminology for Liver Anatomy and Resections. The terminology has added definitions of liver anatomy and resections that were not defined in the Brisbane 2000 system.

KEYWORDS

anatomic liver resection, cone unit, Glissonean approach, segmentectomy, subsegmentectomy

1 | INTRODUCTION

The Brisbane 2000 terminology for liver anatomy and resections[1] is the most common nomenclature system to define and classify hepatectomies worldwide.[2] In this system, Couinaud's anatomical description serves as the backbone for the classification of resections.[3] Anatomical parts of the liver were clearly defined by the portal ramifications: the first-order division is "hemi-liver," the second-order division is "section," and the third-order division is "segment." However, the Brisbane 2000 system did not address anatomic resections of less than one segment. Moreover, despite the studies carried on by Couinaud on liver casts and cadavers, which identified segments 1 through 8, anatomical segmentectomies were not precisely described in the classification. Because the borders between segments were not clearly defined, the definition of segmentectomy in the Brisbane 2000 system does not seem practically feasible.

Minimally invasive liver resection (MILR) has gained widespread popularity after two consensus meetings[4,5] and one guideline meeting.[6] Furthermore, the recent advancements in high-resolution cameras with infrared technology enable even more precise MILR. MILR is theoretically better than open liver resection with better exposure and less bleeding due to pneumoperitoneal pressure.[7] Precise MILR makes parenchymal sparing anatomical resections possible, including sectionectomy, segmentectomy, and subsegmentectomy.[5] These are complex resections that require the identification of anatomical boundaries.

Takasaki's concept[8] is probably the most accepted and recognized alternative to Couinaud's classification and differs from this in many aspects. Indeed, he first reported a technique for open anatomical right lateral sectionectomy, transecting the Glissonean pedicle and naming the procedure as the Glissonean approach.[9] Subsequently, he noticed that the area fed by the tertiary branches of the portal vein had the shape of a cone, and he, therefore, named the resection of the most distal portal ramification as "cone unit" resection.[10] Thus, the concept of cone unit is specific to this nomenclature. Later, Takasaki described the Glissonean pedicle isolation application even for limited hepatic resection as subsegmentectomy, approaching the 2nd and the 3rd order Glissonean branches.[8]

The PAM-HBP Surgery Consensus was held online as the special program of the 32nd meeting of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS) in Tokyo on February 23rd and 24th, 2021, sponsored by JSHBPS and endorsed by the International Hepato-Pancreatic-Biliary Association (IHPBA) and the International Laparoscopic Liver Society (ILLS). We originally planned to hold it in person in June 2020. However, it was postponed and became online due to the COVID-19 pandemic. One of the consensus aims was to update the Brisbane 2000 terminology for liver anatomy and resections, incorporating Takasaki's concept and the definitions of anatomic segmentectomy and subsegmentectomy. The Tokyo 2020 terminology for liver anatomy and resections presents the definitions and the recommendations formulated in the PAM-HBP Surgery Consensus terminology subgroup shown in Table S1. The purpose of this paper is to present that terminology.

2 | METHODS

In June 2019, at the Board of Directors meeting of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS), the PAM-HBP Surgery Consensus was approved to be held as a special session at the 32nd meeting of JSHBPS in June 2020. The Steering Committee (SC) invited 34 international experts around the world. The Expert Committee (EC) subgroup selected 12 questions and two future research topics to be answered in

the terminology session. In addition, the subgroup of EC created seven tentative definitions and five tentative recommendations based on the experts' opinions and the literature review performed by the Research Committee (RC). Finally, two Delphi Rounds finalized those definitions and recommendations.

To analyze currently available evidence regarding the terminology, the RC used the search strategy shown in Table S2. A total of 201 manuscripts were found, from which 175 were outright discarded as they were not directly related to our clinical questions in terminology or were case reports with a poor level of evidence or no added value with the current topic. From the subset of included manuscripts, only 26 manuscripts (no systematic reviews/meta-analyses/controlled studies, one comparative study[11] which did not specifically address our endpoints) were focused on the topic. The RC further analyzed them according to the Scottish Intercollegiate Guidelines Network (SIGN) methodology. Twenty-five manuscripts were analyzed, representing retrospective single center experience and/or experts' opinion on the topic of the Consensus.[8,12-14] The summary of definitions and recommendations for terminology is shown with included literature and the respective SIGN scores and voting rate in Table S3.

Four experts in open liver surgery and liver transplantation were selected to compose the Validation Committee (VC) for the consensus. VC members did not participate in creating definitions and recommendations but were invited to comment freely during the meeting's sessions. The final recommendations and the manuscript were reviewed and approved by all the experts and the validation committees before publication.

3 | WHAT IS ANATOMIC LIVER RESECTION?

Definition 1: Anatomic liver resection (ALR) is defined as the complete removal of the liver parenchyma confined within the responsible portal territory.

According to the Brisbane terminology, ALRs are defined as segmentectomy, sectionectomy, sectorectomy, hemihepatectomy, trisectionectomy. Many papers in the literature also refer to hemihepatectomy as hepatic lobectomy. Portal ramifications clearly defined anatomical portions of the liver. The first-order division defines the "hemi-liver," the second-order division defines the "section," while the third-order division defines the "segment." The hepatic artery, bile duct, and portal vein watersheds are identical except for the second-order division of these structures on the left side of the liver. The portal vein watershed divides the left side of the liver through the plane between segments 2 and 3. Couinaud used the portal veins' ramification as the basis of division to divide the liver, while Healey used the hepatic arteries and bile ducts. In Brisbane 2000 terminology, it was considered reasonable to look for guidance to the arteries and bile ducts in the left side of the liver since it has not been modified for fetal needs.[15] The falciform ligament separates the left lateral section and the left medial section in the left liver. In contrast, the left portal vein ramifies into the left lateral and left medial sectors (OR left paramedian sectors).

Hepatic veins coursing the intersegmental planes are defined as intersegmental/sectional veins. Main hepatic veins have been significant landmarks between the hemilivers and between the sections. However, in approximately half of the patients, the right hepatic vein does not always run along the right intersectional plane.[16,17] This is important especially when performing left trisectionectomy or central bisectionectomy.

The hepatic vein-guided approach is helpful for MIALR using the Glissonean approach because these veins can be used as landmarks to divide the liver parenchyma. However, ALR cannot be defined as completely removing the liver parenchyma confined within the respective hepatic veins.

Definition 2: Anatomical segmentectomy is defined as the complete removal of a territory (territories) of the third-order portal venous branches of a Couinaud segment.

The term "segment" is restricted to the third-order division as described by Couinaud.[3] Couinaud segments defined by the third-order branching provide a road map that is widely understood and accepted. However, segmentation is approximative, different between individuals, and only specific 3D preoperative reconstructions and intraoperative selective clamping/staining can precisely define segmental borders for different patients. Surgeons can identify contiguous territories of the third-order portal branches to resect and name these responsible branches, taking the relations with Couinaud's liver segmentation into account, preferably using a 3D simulation of the portal tree. The intersegmental planes between segments must be visualized by ICG staining (negative/positive) to perform precise anatomical segmentectomy. An alternative way to perform anatomic segmentectomy is to expose and follow the intersegmental veins running between segments differentiated by the surface demarcation without ICG staining. Furthermore, the Glissonean approach is another approach to effectively take the third-order portal territories (Glissonean pedicles) and perform anatomical mono-segmentectomy.[8] One segment consists of one to several third-order portal territories (Figure 1). A

laparoscopic mono-segmentectomy of Sg 5 composed of three separate cone units is shown in Video S1.

Definition 3: Anatomical subsegmentectomy is defined as the removal of the liver parenchyma within the portal territory (territories) of less than a Couinaud's segment. These are also defined as cone units, and their areas can be intraoperatively assessed by using ischemic demarcation, ICG (negative/positive) staining, or both.

The term "subsegmentectomy," originally introduced for small hepatocellular carcinomas by Makuuchi et al.,[18] is the systematic removal of the liver area confined within tumor-bearing portal tributaries. In clinical practice, it is reasonable to define ALR less than sectionectomy as a combination of contiguous territories of the third-order portal venous branches smaller than one Couinaud's segment, compared to the removal of Couinaud's segments are based on a simple spatial segmentation.[19] Therefore, the concept of "cone-unit" was proposed for the third- or higher-order peripheral Glissonean pedicles to define the anatomical area in the PAM-HBP Surgery Consensus. This proposal was agreed upon by almost all the members of EC (97.1%). Cone-unit is the smallest anatomical area based on the portal ramification. Figure 2A shows a pre-operative simulation of three cone units' resection. A subsegment of Sg 6 is the fourth-order portal territory (Figure 2B) and a laparoscopic Sg 6 subsegmentectomy (one cone unit) + Sg 7 segmentectomy is shown in Video S2.

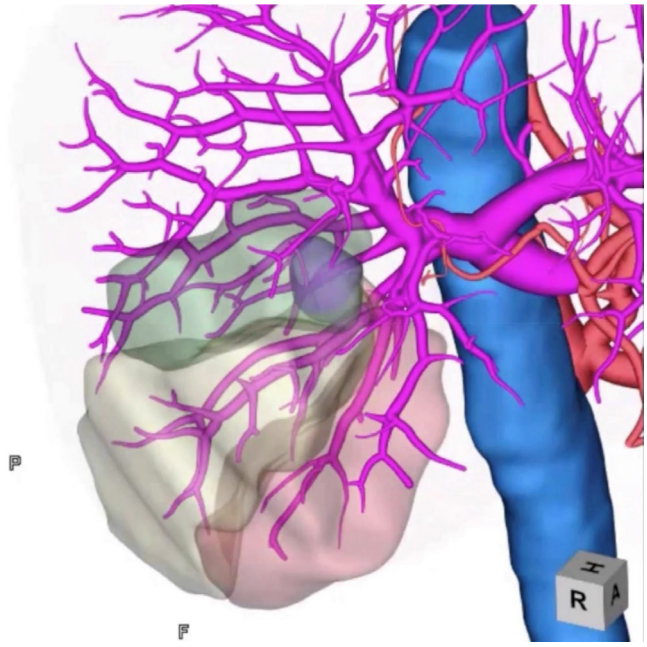

FIGURE 1 Sg 5 consists of three cone units. Pre-operative simulation of Sg 5 mono-segmentectomy clearly shows Sg 5 consists of three cone units. Sg 5 lateral is in yellow, Sg 5 cranial in green, and Sg 5 caudal in red. A laparoscopic Sg 5 mono-segmentectomy (composed of three cone units) is shown in Video S1

Definition 4: A subsegment is an anatomical portion of a Couinaud segment, which is defined as a cone unit or cone units, based on subsegmental inflow. This concept particularly adapts to Sg 8 (ventral and dorsal), Sg 4 (basal and apical), and Sg 1 (Spiegel, caudate process, and paracaval).

The extent of resection is defined by adding and withdrawing the resected territories' number, taking the surgical margin, and remaining liver function into consideration. As a segment consists of one to several third-order portal territories, subsegments are defined as groups of cone units. Parenchymal sparing resection is essential for safe liver surgery. Moreover, preservation of the remnant liver volume allows for re-resection in case of recurrence. Besides formal right and formal left hepatectomy, anatomical resection refers to parenchymal preserving resections of portal territories, including sectionectomy, segmentectomy, and subsegmentectomy. In clinical practice, Sg 8 can be divided into Sg 8 ventral and dorsal and more by the portal ramification because Sg 8 is usually the largest segment of the liver. Similarly, Sg 4 consists of Sg 4a (cranial part subsegment) and 4b (caudal part subsegment), and Sg 1 consists of three subsegments: the Spiegel lobe, the caudate process, and the paracaval portion. However, in surgical practice, we need to visualize these boundaries between subsegments using ICG or dye segmentation techniques.

Definition 5: Sg 4 is redefined as consisting of two subsegments: Sg 4a (apical) and 4b (basal). Sg 4a is defined as the cranial anatomical portion of Sg 4 according to the third-order portal territories, and Sg 4b is the caudal anatomical portion of Sg 4.

According to the arteries and bile ducts, Healey and Schroy divided the medial segment (equivalent to the left medial section or Sg 4 in Brisbane 2000 terminology) into superior and inferior areas.[20] Other conventional divisions of Sg 4, such as 4a (apical) and 4b (basal), also play an important role in defining ALR of less than the entire Sg 4. There is another subsegment located beneath the falciform ligament, defined as Sg 4c. It is supplied by a Glissonean pedicle branching from behind the umbilical portion to the middle cranial part of Sg 4. If a Glissonean approach is performed for segments 2 and 3 branches, the border between the left lateral section and the medial section, which is the falciform ligament, is not the same as the demarcation line because of the area of subsegment 4c.

Definition 6: Sg 9 definition of the BRISBANE 2000 terminology is abandoned, and the caudate lobe is redefined based on portal ramifications instead of spatial recognition.

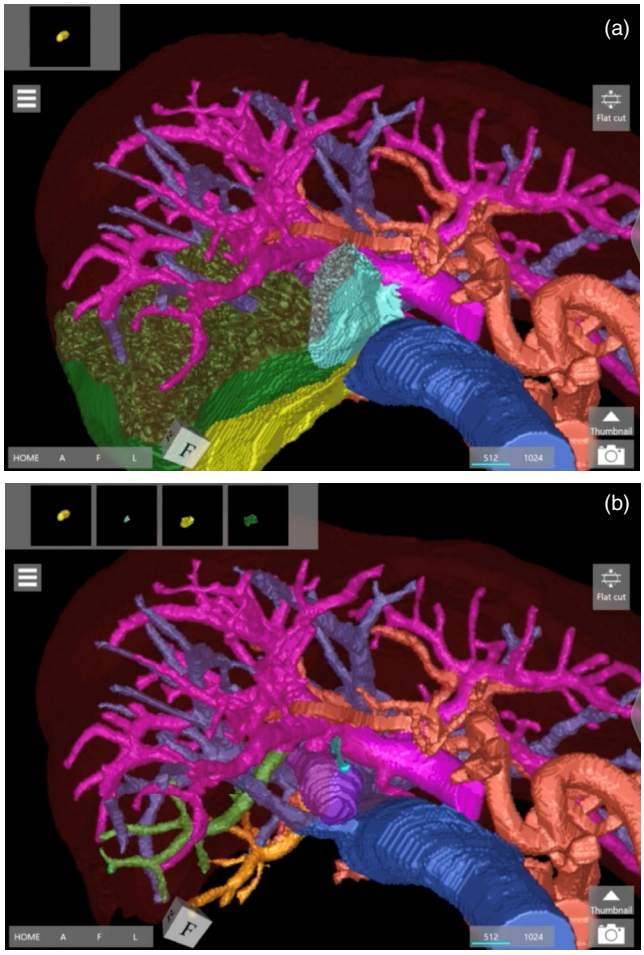

FIGURE 2 Pre-operative simulation of three cone units resection. Part A shows a pre-operative simulation of resection of a caudate process in blue, Sg 7 in yellow, and subsegment of Sg 6 in green. Part B shows Glissonean branches of Sg 6 (G6), Sg 7 (G7), a caudate process (G1c), and a tumor in purple. The fourth-order portal branch shown in green is in charge of a subsegment of Sg 6. A laparoscopic Sg 6 subsegmentectomy (one cone unit) + Sg 7 mono-segmentectomy is shown in Video S2

In 1994, Couinaud defined that the dorsal part of the liver in front of the inferior vena cava which was divided into segment I (left side), which included the caudate lobe, and segment IX (right side), which was incorporated in the posterior surface of the right liver.[21] He later abandoned this definition, publishing an updated paper in 2002.[22] While Couinaud described segments II through VIII based on portal segmentation, his definition of the dorsal liver is only based on spatial anatomy and not on portal segmentation. Thus, the Couinaud's classification lacks consistency in terms of the caudate lobe anatomy. Kumon et al. defined Sg 1 as an anatomical liver portion supplied by the portal vein branches coming off the first order (right portal vein, left portal vein, or trunk).[23] Through his great liver cast works, he proposed a clinically useful subsegmental anatomy of Sg 1, consisting of three parts, the Spiegel lobe, the paracaval portion, and the caudate process, each of which has its own single or multiple corresponding and independent portal vein feeders.[24]

Definition 7: The anatomy of Sg 1 is classified into three parts as follows, I) the spiegel lobe, II) the paracaval portion, and III) the caudate process.

The caudate portal branches should be defined as dorsal branches from the main trunk or first-order branches of the portal vein feeding the liver parenchyma in front of the inferior vena cava (Figure 3). The Spiegel portal branches are dorsal portal branches ramified to the left-sided caudate lobe from the main trunk or the first order portal branches. The paracaval portal branches are dorsal cranial portal branches ramified from the main trunk or the first order portal branches, including branches having a common trunk with Spiegel branches but excluding ventral branches. The Arantius' ligament is a significant landmark showing the boundary between the Spiegel lobe and the paracaval portion. However, the boundary between the paracaval portion and the posterior segment is invisible without a clear landmark. ICG or dye segmentation should be used to visualize these boundaries. The branches of the caudate process are defined as dorsal, caudal portal branches ramified from the main trunk or the first-order branches of the right portal vein. In

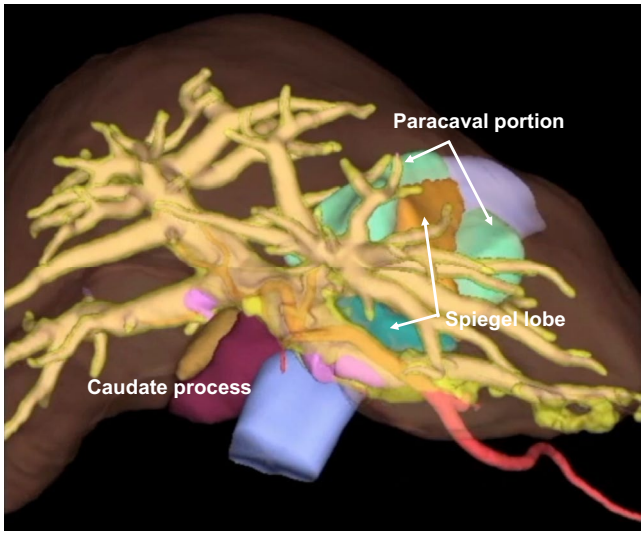

FIGURE 3 Sg 1 consists of three areas and four portal territories. The pre-operative simulation of Sg 1 shows four different portal territories in this patient. Glissonean branches of Sg 1 are the Spiegel portal branches, the paracaval portal branches, and the caudate process branches. This patient has two Spiegel portal branches (G1l superior in yellow and G1l inferior in dark green), the paracaval portal branch (G1r in light green), and the caudate process branch (G1c in red). A laparoscopic mono-segmentectomy of Sg 1 of this patient is shown in Video S3

cases with a trifurcated type of portal vein, the caudate portal branches ramify from the main portal trunk of the portal vein and not from the anterior or posterior portal vein.[24] A laparoscopic mono-segmentectomy of Sg 1 using the Glissonean approach is shown in Video S3, and a robotic-assisted mono-segmentectomy of Sg 1 is shown in Video S4.

Recommendation 1: The terms "segmentectomy and subsegmentectomy" should not be used for non-anatomical resections.

We have defined anatomical segmentectomy and anatomical subsegmentectomy as described above. Even though the Brisbane 2000 terminology also defined segmentectomy, there is no description of the Glissonean approach, the dye injection into the portal vein, and the ICG staining (negative/positive). It is impossible to perform anatomical segmentectomy or subsegmentectomy without the Glissonean approach, the dye injection into the portal vein, and/or the ICG staining (negative/positive). Therefore, as described in the Brisbane 2000 terminology, these segmentectomies were partial resection or wedge resection of the area defined spatially using the term "segments 1 to 8." To avoid confusion, we should not use segmentectomy and subsegmentectomy for non-anatomical resection.

Recommendation 2: To perform segmentectomies or subsegmentectomies, there are two main approaches to the responsible Glissonean pedicle either from the hilum or from the liver surface, depending on the tumor's location and the surgeon's experience.

Branching of the Glissonean pedicles can be followed and visualized from the hilum. For segments 1, 2, 3, 4, 5, 6, the roots of these Glissonean pedicles locate close to the hilum. In contrast, the roots of the Glissonean pedicles for segments 8 and 7 locate a couple of centimeters deeper from the hilum. If you divide the liver parenchyma behind the cystic plate and between segments 6 and the caudate process, the roots of the Glissonean pedicles for segments 8 and 7 can be visualized easily. However, the locations of these Glissonean branches differ among patients, and pre-operative simulation to plan the approach to the Glissonean pedicles is recommended.

Recommendation 3: For a precise segmentectomy or subsegmentectomy, it is recommended to use color dye or indocyanine green dye through either systemic injection under the Glissonean pedicle clamping/occlusion (negative staining) or direct portal vein injection (positive staining) for the visualization of the territory of the responsible portal veins.

The borders between segments cannot be identified appropriately unless dye injection to the responsible portal veins and ICG staining (negative/positive) are used. The color dye injection was first reported in 1985 to perform segmentectomy and subsegmentectomy to identify the surface borders.[18] Before ICG staining, segmentectomies were more performed intentionally using external landmarks (gallbladder, hepatic vein roots, round/falciform ligament), intraoperative ultrasound, intersegmental hepatic vein guidance, and selective inflow clamping with or without dye (indigo carmine or methylene blue dye injection). However, while those methods were precise on the liver surface, they became more uncertain in deeper parenchymal dissection. The advent of ICG staining has been a complete game-changer by allowing precise anatomical delineation for both the surface and the inner parts of the liver. As a result, recent advancements with the ICG technology enables visualization of the intersegmental/sectional planes to perform precise MIALR.[25] Compared with the positive staining technique, the negative staining technique for identifying the area of the responsible Glissonean pedicle is simpler and more feasible.[26] The direct ICG injection into a portal vein branch, particularly in the setting of MIALR, requires the sophisticated manipulation of the needle and careful injection under the appropriate guidance with IOUS, therefore requiring specific skills.

Recommendation 4: Following the appropriate intersegmental/sectional plane is the key to perform precise anatomic liver resection.

Once we follow the cone unit concept, any part of the liver can be divided anatomically. The liver consists of eight segments, consisting of one to several third-order portal territories or cone units. Furthermore, these cone units can be divided even further into smaller cone units consisting of the fourth-order (or more) portal territories.

Therefore, the liver resection can be planned freely by adding these cone units or removing them to ideally cover the tumor-bearing area for anatomic resection. These complex liver resections need the visualization of the intersegmental/sectional planes because anatomical borders between segments and subsegments are not visible. For this purpose, the ICG technology enables the visualization of these anatomical borders deep inside the liver parenchyma, allowing to follow these planes much easier.

Recommendation 5: The intersegmental/sectional plane contains hepatic veins running along the plane or crossing the planes.

Major hepatic veins, which run in the boundaries between the anatomical sections or segments, are critical internal landmarks during the liver transection. The middle hepatic vein runs along the midplane of the liver. The branching veins from segments 5 and 8 are merging from the right hemi-liver, and the veins from Sg 4 are merging from the left hemi-liver. These merging veins are crossing

the midplane of the liver but also course along the plane. Therefore, only veins will be encountered while performing precise ALR following the intersegmental/sectional planes. Careful parenchymal transection is needed to avoid bleeding from these veins. The right hepatic vein runs along the right lateral plane, separating the right anterior and posterior sectors. As described previously, however, in approximately a half of patients, the right hepatic vein does not always run along the right intersectional plane.[16,17] Likewise, the left hepatic vein separates segments 2 and 3.

Future research topic 1: We defined segmentectomy as the complete removal of a territory(territories) of the third-order portal venous branches. The number and direction of these portal venous branches differ among segments 1 to 8. Therefore, these portal venous branches should be studied in terms of the number and direction in each segment. Generally, three to four portal venous branches exist in segments 5 and 8. It would be nice to name these branches such as S8 dorsal, S8 ventral, S5 lateral, S5 cranial, and so on.

The terminology of S8 dorsal and S8 ventral are usually widely accepted. On the other hand, Sg 5 territory is small compared to Sg 8 territory. Furthermore, the terminology of S5 lateral and S5 cranial are not widely used. Further study is needed to determine if these subsegments can be classified in Sg 5. Given the anatomic variants, a specific reproducible definition of all segments may be non-practical. However, those segments with constant subsegmental division should be studied and defined.

Future research topic 2: We defined subsegment as an anatomical portion of a Couinaud segment. It should be studied and defined if subsegments also consist of third-order portal territories or fourth-order portal territories.

As Video S1 shows that Sg 5 consists of three cone units, a subsegment can be two cone units out of these three, the third-order portal territories, for example. However, if a segment consists of one third-order portal territory, the subsegment of such segment should consist of the fourth-order portal territories. Given the study described above, we should know the patterns of subsegment in each segment. It should also be defined how feasible and reproducible are subsegmentectomies for each of the Couinaud segments. For surgical practice, future research should focus on those issues to better understand the anatomy and performance of the surgical procedures. In addition, our newly developed definitions will require a novel notation system, which will hopefully be integrated with the "New World" terminology recently proposed by Nagino et al.[27]

4 | SUMMARY OF DEFINITIONS

Definition 1: Anatomic liver resection (ALR) is defined as the complete removal of the liver parenchyma confined within the responsible portal territory.
Definition 2: Anatomical segmentectomy is defined as the complete removal of a territory (territories) of the third-order portal venous branches of a Couinaud segment.
Definition 3: Anatomical Subsegmentectomy is defined as the removal of the liver parenchyma within the portal territory (territories) of less than a Couinaud's segment. These are also defined as cone units, and their areas can be intraoperatively assessed by using ischemic demarcation, ICG (negative/positive) staining, or both.
Definition 4: A subsegment is an anatomical portion of a Couinaud segment, which is defined as a cone unit or cone units, based on subsegmental inflow. This concept particularly adapts to Sg 8 (ventral and dorsal), Sg 4 (basal and apical), and Sg 1 (Spiegel, caudate process, and paracaval).
Definition 5: Sg 4 is redefined as consisting of two subsegments: Sg 4a (apical) and 4b (basal). Sg 4a is defined as the cranial anatomical portion of Sg 4 according to the third-order portal territories, and Sg 4b is the caudal anatomical portion of Sg 4.
Definition 6: Sg 9 definition of the Brisbane 2000 terminology is abandoned, and caudate lobe is redefined based on portal ramifications instead of spatial recognition.
Definition 7: The anatomy of Sg 1 is classified into three parts as follows, i) the Spiegel lobe, ii) the paracaval portion, and iii) the caudate process.

5 | SUMMARY OF RECOMMENDATIONS

Recommendation 1: The terms "segmentectomy and subsegmentectomy" should not be used for non-anatomical resections.
Recommendation 2: To perform segmentectomies or subsegmentectomies, there are two main approaches to the responsible Glissonean pedicle either from the hilum or from the liver surface, depending on the tumor's location and the surgeon's experience.
Recommendation 3: For a precise segmentectomy or subsegmentectomy, it is recommended to use color dye or indocyanine green dye through either systemic injection under the Glissonean pedicle clamping/occlusion (negative staining) or direct portal vein injection (positive staining) for the visualization of the territory of the responsible portal veins.

Recommendation 4: Following the appropriate intersegmental/sectional plane is the key to perform precise anatomic liver resection.

Recommendation 5: The intersegmental/sectional plane contains hepatic veins running along the plane or crossing the planes.

ACKNOWLEDGMENTS

This project was conducted as a project study of JSHBPS. All authors acknowledge the financial support from JSHBPS, and the endorsement from IHPBA. Details on the design of this project were decided by Go Wakabayashi, Daisuke Ban, Yuichi Nagakawa, Takao Ohtsuka, Minoru Tanabe, Masafumi Nakamura, Akihiko Tsuchida. The systematic review was supervised by Ruben Ciria, Giammauro Berardi, Hitoe Nishino, and performed by Felipe Alconchel, Keiichi Akahoshi, Shunichi Ariizumi, Andrea Benedetti Cacciaguerra, Manuel Durán, Alain García Vázquez, Nicolas Golse, Yoshihiro Miyasaka, Yasuhisa Mori, Satoshi Ogiso, Chikara Shirata, Federico Tomassini, Takeshi Urade, and Taiga Wakabayashi. Survey was conducted with the help of Filipe Kunzler. The clinical questions and recommendations were formulated and voted by 34 expert committee members; Yuta Abe, Mohammed Abu Hilal, Takeshi Aoki, Horacio J. Asbun, Giammauro Berardi, Albert CY Chan, Rawisak Chanwat, Kuo-Hsin Chen, Yajin Chen, Daniel Cherqui, Tan To Cheung, Ruben Ciria, David Fuks, David A. Geller, Naoto Gotohda, Ho-Seong Han, Kiyoshi Hasegawa, Etsuro Hatano, Goro Honda, Osamu Itano, Yukio Iwashita, Hironori Kaneko, Yutaro Kato, Ji Hoon Kim, Rong Liu, Santiago López-Ben, Kazuteru Monden, Mamoru Morimoto, Fernando Rotellar, Yoshihiro Sakamoto, Atsushi Sugioka, Minoru Tanabe, Go Wakabayashi, and Tomoharu Yoshizumi. Hitoe Nishino, Shingo Kozono, Hiroaki Osakabe, and Chie Takishita contributed to the progress of this project as the secretariat. The draft of the manuscript was critiqued by all 34 expert committee members and four validation committee members; Taizo Hibi, Norihiro Kokudo, Masayuki Ohtsuka, and Masakazu Yamamoto. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

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How to cite this article: Wakabayashi G, Cherqui D, Geller DA, Abu Hilal M, Berardi G, Ciria R, et al. The Tokyo 2020 terminology of liver anatomy and resections: Updates of the Brisbane 2000 system. J Hepatobiliary Pancreat Sci. 2022;29:6–15. https://doi.org/10.1002/jhbp.1091

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