工藤正俊業績

超音波造影法の開発と臨床応用の研究

1980 年代に入り、それまでのコンタクトコンパウンド方式から電子スキャンが開発され超音波検査は画期的な進歩を遂げた。それにより、超音波で肝臓内に小さな結節が多数検出されるようになったが、慢性肝疾患や肝硬変の患者に小さな 1～2cm 大の結節が見つかっても血管造影による精査でも質的診断不可能な結節性病変が多数増加し日本国内のみならず、世界的に大きな問題となってきていた。当時は MDCT や MRI などの腹部応用がまだ進んでおらず、腫瘍生検による病理診断が唯一、肝の微小結節性病変診断法の主流であった。

工藤正俊は超音波のみで検出され、血管造影では濃染を呈さないような結節に対して無菌的に採取した CO2 と自家血の用手撹拌により作成した CO2 マイクロバブルを、肝動脈内に挿入したカテーテル先端から注入し、対外からの超音波検査でそのような微小結節内の CO2 マイクロバブルを含む血流の輝度上昇を検出することにより結節内の動脈血流が増加しているのか低下しているのか、あるいは周囲肝と同程度であるかといった**血流動態の評価を可能にする画期的な手法（CO2 マイクロバブル動注による CO2 動注 Angiography［超音波造影法］）を開発した。この手法は肝腫瘍の超音波造影法としては世界初の検査法の開発であった。**この手法は結節内の動脈血流の多寡を検出することにより病理学的早期肝癌の診断を可能にするのみならず、結節内の血管構築を正確に評価できることから、肝細胞癌、転移性肝癌、胆管細胞癌、血管腫、FNH などの鑑別診断も可能にする画期的な手法である。さらには、門脈造影下 CT と併用することにより肝硬変にともなう結節性病変の結節内血流動態評価による悪性度評価にも応用できることを証明した。工藤正俊がこの手法を考案したのは、米国カリフォルニア大学のデイビスメディカルセンター（UC Davis）から帰国した 1989 年であるが、以降、次々に英文論文として発表したため世界からこの手法に注目が集まるようになった。この論文をきっかけに世界中に**静注造影超音波法**開発のニーズが高まってきた。その結果、この CO2 動注 US angio 法開発の延長線上として 1999 年、第一世代の超音波造影剤レボビストの開発につながった。レボビストの開発においても工藤正俊は中心的な役割を果たし独シェーリング社との共同開発により治験を成功させレボビストを保険承認に導いた。更には第二世代の超音波造影剤であるソナゾイド造影超音波の開発を第一三共株式会社（現剤、GE Healthcare）と開始し、2007 年治験を成功させることによりソナゾイドが静注用超音波造影剤として薬事承認された。また、ソナゾイドのみにおいて可能な Defect Reperfusion 法（Re-injection technique）も開発しこの手法は世界各国でルーチンのテクニックとして使用されている。

その後、ソナゾイド造影超音波は膵臓の腫瘍性病変の鑑別などにも近畿大学において世界で初めて臨床応用され、多くの英文論文発表を行い、超音波造影法を確立した。ソナゾイドは 2012 年頃までは日本でのみ使用可能であったが、現在では世界各地でソナゾイドに対するニーズが高まり、中国、台湾、韓国、ノルウェーなどの各国で次々と承認されるに至っている。

2013 年には工藤正俊が世界超音波医学会（WFUMB）の理事長であった時に造影エコー法の世界のガイドラインを発表したが、この論文の引用件数は 800 回以上にも及んでいる。また、最近 WFUMB により改訂され 2020 年に発表された肝臓の造影超音波法の改訂版の主要メンバーとしても参画している。すなわち造影超音波法の開発、普及、ガイドライン作成のそのすべてに工藤正俊は携わった。

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1. Kudo M*, Tomita S, Tochio H, Kashida H, Hirasa M, Todo A: Hepatic focal nodular hyperplasia: specific findings at dynamic contrast-enhanced ultrasonography with carbon dioxide microbubbles. **Radiology** 179: 377-382, 1991. **(IF= 7.931)**

2. Kudo M*, Tomita S, Tochio H, Mimura J, Okabe Y, Kashida H, Hirasa M, Ibuki Y, Todo A: Sonography with intraarterial infusion of carbon dioxide microbubbles (sonographic angiography): value in differential diagnosis of hepatic tumors. **AJR Am J Roentgenol** 158: 65-7, 1992. **(IF=3.013)**

3. Kudo M*, Tomita S, Tochio H, Mimura J, Okabe Y, Kashida H, Hirasa M, Ibuki Y, Todo A: Small hepatocellular carcinoma: diagnosis with US angiography with intraarterial CO2 microbubbles. **Radiology** 182: 155-160, 1992. **(IF= 7.931)**

4. Kudo M*: Morphological diagnosis of hepatocellular carcinoma: special emphais on intranodular hemodynamic imaging. **Hepato-Gastroenterol** 45: 1226- 1231, 1998. (IF=0.792)

5. Kudo M*: Imaging diagnosis of hepatocellular carcinoma and premalignant /borderline lesions. **Semin Liver Dis** 19: 297-309, 1999. **(IF=4.457)**

6. Ding H, Kudo M*, Onda H, Suetomi Y, Minami Y, Maekawa K: Contrast-enhanced subtraction harmonic sonography for evaluating treatment response in patients with hepatocellular carcinoma. **AJR Am J Roentgenol** 176: 661-666, 2001. **(IF=3.013)**

7. Ding H, Kudo M*, Onda H, Suetomi Y, Minami Y, Maekawa K: Hepatocellular carcinoma: depiction of tumor parenchymal flow with intermittent harmonic power Doppler US during the early arterial phase in dual display model. **Radiology** 220: 349-356, 2001. **(IF= 7.931)**

8. Ding H, Kudo M*, Onda H, Nomura H, Haji S: Sonographic diagnosis of pancreatic islet cell tumor: value of intermittent harmonic imaging. **J Clin Ultrasound** 29: 411-416, 2001. **(IF=0.764)**

9. Kudo M*: Imaging blood flow characteristics of hepatocellular carcinoma. **Oncology** 61:48-56, 2001. **(IF=2.642)**

10. Ding H, Kudo M*, Maekawa K, Suetomi Y, Minami Y, Onda H: Detection of tumor parenchymal blood flow in hepatic tumors: value of second harmonic imaging with a galactose-based contrast agent. **Hepatol Res** 21: 242-251, 2001. **(IF=3.165)**

11. Kudo M*: Contrast harmonic ultrasound is a breakthrough technology in the diagnosis and treatment of hepatocellular carcinoma. **J Med Ultrason** 28: 79-81, 2001. **(IF=0.898)**

12. Ding H, Kudo M*, Onda H, Suetomi Y, Minami Y, Chung H, Kawasaki K, Maekawa K: Evaluation of posttreatment response of hepatocellular carcinoma

with contrast-enhanced coded phase-inversion harmonic US: comparison with dynamic CT. **Radiology** 221: 721-730, 2001. **(IF= 7.931)**

13. Wen YL, **Kudo M**, Kawasaki T, Minami Y, Maekawa K: Hepatocellular carcinoma treated with radiofrequency ablation: Evaluation of therapeutic response by contrast-enhanced Coded Harmonic Angio. **Chinese J Ultrasound Med** 18: 452-455, 2002. **(IF=0.000)**

14. **Kudo M***: Radiofrequency ablation for HCC under contrast-harmonic imaging. **J Society Ultrasound Med ROC** 18: 48-50, 2002. **(IF=0.000)**

15. **Kudo M***: Contrast harmonic imaging in the characterization of hepatic tumors. **J Society Ultrasound Med ROC** 18: 52-53, 2002. **(IF=0.000)**

16. Wen YL, **Kudo M**, Luo BM, Maekawa K: Usefulness of different modes of contrast-enhanced power Doppler imaging in assessment of intratumoral vascularity in hepatocellular carcinoma. **Chinese J Ultrasound Med** 18: 773-776, 2002. **(IF=0.000)**

17. Wen YL, **Kudo M***, Maekawa K, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T: Contrast advanced dynamic flow imaging and contrast pulse subtraction imaging: preliminary results in hepatic tumors. **J Med Ultrason** 29: 195-204, 2003. **(IF=0.898)**

18. Minami Y, **Kudo M***, Kawasaki T, Kitano M, Chung H, Maekawa K, Shiozaki H: Transcatheter arterial chemoembolization of hepatocellular carcinoma: usefulness of coded phase-inversion harmonic sonography. **AJR Am J Roentgenol** 180: 703-708. **(IF=3.013)**

19. Wen YL, **Kudo M***, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Assessment of image quality of contrast-enhanced power Doppler imaging in hepatocellular carcinoma with a personal ultrasound imager: comparison with conventional machine. **J Med Ultrason** 30: 31-38, 2003. **(IF=0.898)**

20. Kawasaki T, **Kudo M**, Inui K, Ogawa C, Chung H, Minami Y: Hepatocellular carcinoma mimicking cavernous hemangioma on angiography and contrast enhanced harmonic ultrasonography. A case report. **Hepatol Res** 25: 202-212, 2003. **(IF=3.165)**

21. **Kudo M***, Minami Y: Radiofrequency ablation therapy under harmonic imaging guidance for the recurring cancer after local therapy for HCC: a randomized controlled study with RFA under B-mode guidance. **Ultrasound Med Biol** 29: 145, 2003. **(IF=2.514)**

22. Wen YL, **Kudo M***, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Radiofrequency ablation of hepatocellular carcinoma: therapeutic response using contrast-enhanced coded phase-

inversion harmonic sonography. **AJR Am J Roentgenol** 181: 57-63. **(IF=3.013)**

23. Wen YL, **Kudo M***, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Contrast-enhnaced Agent Detection Imaging: early experience in hepatocellular carcinoma. **J Med Ultrason** 30: 77-84. **(IF=0.898)**

24. Wen YL, **Kudo M***, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Value of new contrast harmonic technique for detecting tumor vascularity in hepatocellular carcinoma: preliminary results. **J Med Ultrason** 30: 85-92. **(IF=0.898)**

25. Wen YL, **Kudo M***, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Detection of tumor vascularity in hepatocellular carcinoma with contrast enhanced Dynamic Flow imaging: comparison with contrast enhanced power Doppler imaging. **J Med Ultrason** 30; 141-151, 2003. **(IF=0.898)**

26. Wang WP, Ding H, Qi Q, Mao F, Xu ZZ, **Kudo M**: Characterization of focal hepatic lesions with contrast-enhanced C-cube gray scale ultrasonography. **World J Gastroetenrol** 9: 1667-1674, 2003. **(IF=3.665)**

27. Wen YL, **Kudo M***, Zheng RQ, Ding H, Minami Y, Chung H, Suetomi Y, Onda H, Kitano M, Kawasaki T, Maekawa K: Characterization of hepatic tumors: value of contrast-enhanced coded phase inversion harmonic US. **AJR Am J Roentgenol** 182: 1019-1026, 2004. **(IF=3.013)**

28. Minami Y, **Kudo M***, Kawasaki T, Chung H, Ogawa C, Shiozaki H: Percutaneous radiofrequency ablation guided by contrast-enhanced harmonic sonography with artificial pleural effusion for hepatocellular carcinoma in the hepatic dome. **AJR Am J Roentgenol** 182: 1224-1226, 2004. **(IF=3.013)**

29. Kitano M, **Kudo M**, Maekawa K, Suetomi Y, Sakamot H, Fukuda N, Nakaoka R, Kawasaki T: Dynamic imaging of pancreatic diseases by contrast-enhanced coded phase- inversion harmonic US. **Gut** 53: 854-859, 2004. **(IF=19.819)**

30. Minami Y, **Kudo M***, Kawasaki T, Chung H, Ogawa C, Shiozaki H: Treatment of hepatocellular carcinoma with percutaneous radiofrequency ablation: usefulness of contrast harmonic sonography for lesions poorly defined with B-mode sonography. **AJR Am J Roentgenol** 183: 153-156, 2004. **(IF=3.013)**

31. Wen YL, **Kudo M***: Detection of the intratumoral vascularity in small hepatocellular carcinoma by coded phase inversion harmonics. **Intervirology** 47: 169-178, 2004. **(IF=1.235)**

32. **Kudo M***: Atypical large well-differentiated hepatocellular carcinoma with benign nature: a new clinical entity. **Intervirology** 47: 227-237, 2004. **(IF=1.235)**

33. Zheng RQ, **Kudo M***: Hepatocellular carcinoma with nodule in nodule appearance: demonstration by contrast-enhanced coded phase-inversion harmonic imaging. **Intervirology** 47: 184-190, 2004. **(IF=1.235)**

34. Fukuta N, Kitano M, Maekawa K, Chikugo T, **Kudo M***: Estimation of the malignant potential of gastrointestinal stromal tumors: The value of contrast-enhanced coded phase-inversion harmonic US. **J Gastroenterol** 40: 247-255, 2005. **(IF=6.132)**

35. Zheng RQ, **Kudo M**: Hepatic angiomyolipoma: identification of an efferent vessel to be hepatic vein by contrast-enhanced harmonic ultrasound. **Br J Radiol** 78: 956-960, 2005. **(IF=2.196)**

36. Zheng RQ, **Kudo M***, Ishikawa E, Chung H, Minami Y, Ogawa C, Sakaguchi Y, Kitano M, Kawasaki T, Maekawa K: Hepatic angiomyolipma: identification of an efferent vessel to be hepatic vein by contrast-enhanced harmonic ultrasonography. **J Med Ultrason** 32: 191-196, 2005. **(IF=0.898)**

37. Sakaguchi Y, **Kudo M***, Zheng RQ, Chung H, Minami Y, Ogawa C, Kitano M, Kawasaki T, Maekawa K: Hemodynamic and morphologic changes of peripheral hepatic vasculature in chronoic liver disease: a preliminary study by contrast-enhanced coded phase-inversion harmonic sonography. **J Med Ultrason** 32: 197-204, 2005. **(IF=0.898)**

38. Inoue T, **Kudo M***, Watai R, Zhou P, Kawasaki T, Minami Y, Chung H, Fukunaga T, Awai K, Maenishi O: Differential diagnosis of nodular lesions in cirrhotic liver by post-vascular phase contrast-enhanced US with Levovist: comparison with superparamagnetic iron oxide magnetic resonance images. **J Gastroenterol** 40: 1139-1147, 2005. **(IF=6.132)**

39. Zheng RQ, Zhang B, **Kudo M**, Sakaguchi Y: Hemodynamic and morphologic changes of peripheral hepatic vasculare in cirrhotic liver disease: a preliminary study using contrast-enhanced coded phase inversion harmonic ultrasonography. **World J Gastroenterol** 11: 6348-6353, 2005. **(IF=3.665)**

40. **Kudo M***: Early detection and characterization of hepatocellular carcinoma: value of imaging multistep human hepatocarcinogenesis. **Intervirology** 49: 64-69, 2006. **(IF=1.235)**

41. Minami Y, **Kudo M***, Chung H, Kawasaki T, Yagyu Y, Shimono T, Shiozaki H: Contrast harmonic sonography guided radiofrequency ablation therapy versus B-mode sonography in hepatocellular carcinoma: prospective randomized controlled trial. **AJR Am J Roentgenol** 188: 489-494, 2007. **(IF=3.013)**

42. noue T, Kitano M, **Kudo M***, Sakamoto H, Kawasaki T, Yasuda C, Maekawa K: Diagnosis of gallbladder diseases by contrast-enhanced phase-inversion harmonic ultrasonography. **Ultrasound Med Biol** 33: 353-361, 2007. **(IF=2.514)**

43. **Kudo M***: New sonographic techniques for the diagnosis and treatment of hepatocellular carcinoma. **Hepatol Res** 37: 193-199, 2007. **(IF=3.165)**

44. Zhou P, **Kudo M***, Minami Y, Chung H, Inoue T, Fukunaga T, Maekawa K: What is the best time to evaluate treatment response after radiofrequency ablation of hepatocellular carcinoma using contrast-enhanced sonography? **Oncology** 72: S92-S97, 2007. **(IF=2.642)**

45. Kitano M, Sakamoto H, Matsui U, Ito Y, Maekawa K, Shrenck T V, **Kudo M**: A novel perfusion imaging technique of the pancreas: contrast-enhanced harmonic EUS (with video). **Gastrointest Endsc** 67: 141-150, 2008. **(IF=6.890)**

46. Kitano M, **Kudo M***, Sakamoto H, Nakatani T, Maekawa K, Mizuguchi N, Ito Y, Miki M, Matsui U, Shrenck T V: P

47. reliminary study of contrast-enhanced harmonic endosonography with second-generation contrast agents. **J Med Ultrason** 35: 11-18, 2008. **(IF=0.898)**

48. Hatanaka K, **Kudo M***, Minami Y, Ueda T, Tatsumi C, Kitai S, Takahashi S, Inoue T, Hagiwara S, Chung H, Ueshima K, Maekawa K: Differential diagnosis of hepatic tumors: value of contrast-enhanced harmonic sonography using the newly developed contrast agent, Sonazoid. **Intervirology** 51: 61-69, 2008. **(IF=1.235)**

49. Sakamoto H, Kitano M, Suetomi Y, Maekawa K, Takeyama Y, **Kudo M**: Utility of contrast-enhanced endoscopic ultrasonography for diagnosis of small pancreatic carcinomas. **Ultrasound Med Biol** 34: 525-532, 2008. **(IF=2.514)**

50. **Kudo M***, Hatanaka K, Maekawa K: Sonazoid-enhanced ultrasound in the diagnosis and treatment of hepatic tumors. **J Med Ultrasound** 16: 130-139, 2008. **(IF=0.000)**

51. Madan K, **Kudo M***, Fukuta N: Multistep progression from a hypovascular nodule to a nodule-in-nodule type hepatocellular carcinoma in hepatitis C-related cirrhosis. **Indian J Gastroenterol** 27: 176, 2008. **(IF=1.080)**

52. Hatanaka K, **Kudo M***, Minami Y, Maekawa K: Sonazoid-enhanced ultrasonography for diagnosis of hepatic malignancies: comparison with contrast-enhanced CT. **Oncology** 75: S42-47, 2008. **(IF=2.642)**

53. Inoue T, **Kudo M***, Hatanaka K, Takahashi S, Kitai S, Ueda T, Ishikawa E, Hagiwara S, Minami Y, Chung H, Ueshima K, Maekawa K: Imaging of hepatocellular carcinoma: qualitative and quantitative analysis of post-vascular phase contrast-enhanced US with Sonazoid; comparison with superparamagnetic iron oxide magnetic resonance images. **Oncology** 75: S48-54, 2008. **(IF=2.642)**

54. **Kudo M***, Tochio H: Intranodular blood supply correlates well with biological malignancy grade determined by tumor growth rate in pathologically proven hepatocellular carcinoma. **Oncology** 75: S55-64, 2008. **(IF=2.642)**

55. Xia Y, **Kudo M***, Minami Y, Hatanaka K, Ueshima K, Chung H, Hagiwara S, Inoue T, Ishikawa E, Kitai S, Takahashi S, Tatsumi C, Ueda T, Hayaishi S, Maekawa K: Response evaluation of transcatheter arterial chemoembolizaion in hepatocellular carcinomas: the usefulness of Sonazoid-enhanced harmonic

sonography. **Oncology** 75: S99-105, 2008. **(IF=2.642)**

56. **Kudo M***: Multistep human hepatocarcinogenesis: correlation of imaging with pathology. **J Gastroenterol** 44: 112-118, 2009. **(IF=6.132)**

57. Inoue T, **Kudo M***, Maenishi O, Kumata M, Nakashima O, Kojiro M, Maekawa K: Value of liver parenchymal phase contrast-enhanced sonography to diagnose the premalignant and borderline lesions and overt hepatocellular carcinoma. **AJR Am J Roentgenol** 192:698-705, 2009. **(IF=3.013)**

58. Minami Y, **Kudo M***: Contrast-enhanced harmonic ultrasound imaging in ablation therapy for primary hepatocelular carcinoma. **World J Radiol** 31: 86-91, 2009. **(IF=0.000)**

59. **Kudo M***: The 2008 Okuda lecture: Management of hepatocellular carcinoma: from surveillance to molecular targeted therapy. **J Gastroen Hepatol** 25: 439-452, 2010. **(IF=3.437)**

60. Minami Y, **Kudo M***, Hatanaka K, Kitai S, Inoue T, Hagiwara S, Chung H, Ueshima K: Radiofrequency ablation guided by contrast harmonic sonography using perfluorocarbon microbubbles (Sonazoid) for hepatic malignancies: an initial experience. **Liver Int** 30: 759-764, 2010. **(IF=5.175)**

61. **Kudo M***, Hatanaka K, Maekawa K: Newly developed novel ultrasound technique, defect reperfusion ultrasound imaging, using Sonazoid in the management of hepatocellular carcinoma. **Oncology** 78: S40-45, 2010. **(IF=2.642)**

62. Hatanaka K, Chung H, **Kudo M***, Haji S, Minami Y, Maekawa K, Hayaishi S, Nagai T, Takita M, Kudo K, Ueda T, Tatsumi C, Kitai S, Ishikawa E, Yada N, Inoue T, Hagiwara S, Ueshima K: Usefulness of the post-vascular phase of contrast-enhanced ultrasonography with Sonazoid in the evaluation of gross types of Hepatocellular carcinoma. **Oncology** 78: S53-59, 2010. **(IF=2.642)**

63. **Kudo M***, Hatanaka K, Inoue T, Maekawa K: Depiction of portal supply in early hepatocellular carcinoma and dysplastic nodule: value of pure arterial ultrasound imaging in hepatocellular carcinoma. **Oncology** 78: S60-67, 2010. **(IF=2.642)**

64. Andreana L, **Kudo M***, Hatanaka K, Chung H, Minami Y, Maekawa K, Ruggiero G: Contrast-enhanced ultrasound techniques for guiding and assessing response to locoregional treatments for hepatocellular carcinoma. **Oncology** 78: S68-77, 2010. **(IF=2.642)**

65. Minami Y, **Kudo M**: Hepatic malignancies: Correlation between sonographic findings and pathological features. **World J Radiol** 2: 249-256, 2010. **(IF=0.000)**

66. Mita K, Kim SR, **Kudo M**, Imoto S, Nakajima T, Ando K, Fukuda K, Matsuoka T, Maekawa Y, Hayashi Y: Diagnostic sensitivity of imaging modalities for hepatocellular carcinoma smaller than 2cm. **World J Gastroenterol** 16: 4187-4192, 2010. **(IF=3.665)**

67. Xia Y, Kitano M, **Kudo M**, Imai H, Kamata K, Sakamoto H, Komaki T: Characterization of intra-abdominal lesions of undetermined origin by contrast-enhanced harmonic EUS (with videos). **Gastrointest Endosc** 72: 637-642, 2010. **(IF=6.890)**

68. **Kudo M***, Hatanaka K, Kumada T, Toyoda H, Tada T: Double-contrast ultrasound: a novel surveillance tool for hepatocellular carcinoma. **Am J Gastroenterol** 106: 368-370, 2011. **(IF=10.171)**

69. Kitano M, **Kudo M**, Sakamoto H, Komaki T: Endoscopic ultrasonography and contrast-enhanced ultrasonography. **Pancreatology** 11: 28-33, 2011. **(IF=3.629)**

70. Kitano M, Sakamoto H, Komaki T, **Kudo M**: New techniques and future perspective of EUS for the differential diagnosis of pancreatic malignancies; Contrast harmonic imaging. **Digest Endosc** 23: 46-50, 2011. **(IF=4.774)**

71. Alaboudy A, Inoue T, Hatanak K, Chung H, Hyodo T, Kumano S, Murakami T, Moustafa EFA, **Kudo M***: Usefulness of combination of imaging modalities in the diagnosis of hepatocellular carcinoma using Sonazoid-enhanced ultrasound, gadolinium diethylene-triamine-pentaacetic acid-enhanced magnetic resonance imaging, and contrast-enhanced computed tomography. **Oncology** 81: 66-72, 2011. **(IF=2.642)**

72. **Kudo M***: Diagnostic imaging of hepatcocellular carcinoma: Recent progress. **Oncology** 81: 73-85, 2011. **(IF=2.642)**

73. Minami Y, Okumura N, Yamamoto N, Tsuji N, Kono Y, **Kudo M***: Quantification of tumor vascularity with contrast-enhanced ultrasound for early response of transcatheter arterial chemoembolization for hepatocellular carcinoma: a report of three cases. **J Med Ultrason** 39: 15-19, 2012. **J Med Ultrason**

74. Kitano M, **Kudo M**, Yamao K, Takagi T, Sakamoto H, Komaki T, Kamata K, Imai H, Chiba Y, Okada M, Murakami T, Takeyama Y: Characterization of small solid tumors in the pancreas: The value of contrast-enhanced harmonic endoscopic ultrasonography. **Am J Gastroenterol** 107, 303-310, 2012. **(IF=10.171)**

75. Kitano M, Sakamoto H, **Kudo M**: Endoscopic ultrasound: contrast enhancement. **Gastrointest Endosc Clin N Am** 22:349-358, 2012. **(IF=0.000)**

76. Inoue T, **Kudo M***, Hatanaka K, Arizumi T, Takita M, Kitai S, Yada N, Hagiwara S, Minami Y, Sakurai T, Ueshima k, Nishida N: Usefulness of contrast-enhanced ultrasonography to evaluate the post treatment responses of radiofrequency ablation for hepatocellular carcinoma; comparison with dynamic CT. **Oncology** 84:51-57, 2013. **(IF=2.642)**

77. Minami Y, **Kudo M**: Therapeutic response assessment of transcatheter arterial chemoembolization for hepatocellular carcinoma: ultrasonography, CT and MR imaging. **Oncology** 84:58-63, 2013. **(IF=2.642)**

78. Claudon M, Dietrich CF, Choi BI, Cosgrove DO, **Kudo M**, Nolsoe CP, Piscaglia

F, Wilson SR, Barr RG, Chammas MC, Chaubal NG, Chen MH, Clevert DA, Correas JM, Ding H, Forsberg F, Fowlkes JB, Gibson RN, Goldberg BB, Lassau N, Leen EL, Mattrey RF, Moriyasu F, Solbiati L, Weskott HP, Xu HX: Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver-update 2012: a WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. **Ultrasound Med Biol** 39:187-210, 2013. **(IF=2.514)**

79. Claudon M, Dietrich CF, Choi BI, Cosgrove DO, **Kudo M**, Nolsoe CP, Piscaglia F, Wilson SR, Barr RG, Chammas MC, Chaubal NG, Chen MH, Clevert DA, Correas JM, Ding H, Forsberg F, Fowlkes JB, Gibson RN, Goldberg BB, Lassau N, Leen EL, Mattrey RF, Moriyasu F, Solbiati L, Weskott HP, Xu HX: Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver-update 2012: a WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. **Ultraschall Med** 34:11-29, 2013. **(IF=4.966)**

80. **Kudo M***: Early hepatocellular carcinoma: definition and diagnosis. **Liver Cancer** 2:69-72, 2013. **(IF=9.720)**

81. Kitano M, Sakamoto H, **Kudo M**: Contrast-enhanced endoscopic ultrasound. **Dig Endosc** 26:79–85, 2014. **(IF=4.774)**

82. Minami Y, Nishida N, **Kudo M**: Therapeutic response assessment of RFA for HCC: contrast-enhanced US, CT and MRI. **World J Gastroenterol** 20:4160-4166, 2014. **(IF=3.665)**

83. Hatanaka K, Minami Y, **Kudo M***, Inoue T, Chung H, Haji S: The gross classification of hepatocellular carcinoma: usefulness of contrast-enhanced US. **J Clin Ultrasound** 42:1-8, 2014. **(IF=0.764)**

84. Minami Y, **Kudo M**: Ultrasound fusion imaging of hepatocellular carcinoma: a review of current evidence. **Diegst Dis** 32:690-695, 2014. **(IF=2.493)**

85. Minami T, Minami Y, Chishina H, Arizumi T, Takita M, Kitai S, Yada N, Inoue T, Hagiwara S, Ueshima K, Nishida N, **Kudo M***: Combination guidance of contrast-enhanced US and fusion imaging in radiofrequency ablation for hepatocellular carcinoma with poor conspicuity on contrast-enhanced US/fusion imaging. **Oncology** 87:55-62, 2014. **(IF=2.642)**

86. Kitano M, Kamata K, Imai H, Miyata T, Yasukawa S, Yanagisawa A, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for pancreatobiliaty diseases. **Digest Endosc** 27:60-67, 2015. **(IF=4.774)**

87. Sugimoto K, Kim SR, Imoto S, Tohyama M, Kim SK, Matsuoka T, Yano Y, **Kudo M**, Hayashi Y: Characteristics of hypovascular versus hypervascular well-differentiated hepatocellular carcinoma smaller than 2cm - focus on tumor size, markers and imaging detectability. **Digest Dis** 33:721-727, 2015. **(IF=2.493)**

88. Tochio H, Sugahara M, Imai Y, Tei H, Suginoshita Y, Iwasaki N, Sasaki I, Hamada M, Minowa K, Inokuma T, **Kudo M***: Hyperenhanced rim surrounding liver metastatic tumors in the postvascular phase of sonazoid-enhanced

ultrasonography: a histological indication of the presence of Kupffer cells. **Oncology** 89:33-41, 2015. **(IF=2.642)**

89. Minami Y, **Kudo M***: Imaging modalities for assessment of treatment response to nonsurgical hepatocellular carcinoma therapy: Contrast-enhanced US, CT and MRI. **Liver Cancer** 4:106-114, 2015. **(IF=9.720)**

90. **Kudo M***: Defect reperfusion imaging with sonazoid®: a breakthrough in hepatocellular carcinoma. **Liver Cancer** 5:1-7, 2016. **(IF=9.720)**

91. Kamata K, Kitano M, Omoto S, Kadosaka K, Miyata T, Yamao K, Imai H, Sakamoto H, Harwani Y, Chikugo T, Chiba Y, Matsumoto I, Takeyama Y, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for differential diagnosis of pancreatic cysts. **Endoscopy** 48:35-41, 2016. **(IF=7.341)**

92. Inoue T, Hyodo T, Korenaga K, Murakami T, Imai Y, Higaki A, Suda T, Takano T, Miyoshi K, Koda M, Tanaka H, Iijima H, Ochi H, Hirooka M, Numata K,**Kudo M***: Kupffer phase image of Sonazoiod-enhanced US is useful in predicting a hypervascularization of non-hypervascular hypointense hepatic lesions detected on Gd-EOB-DTPA-enhanced MRI: A multicenter retrospective study. **J Gastroenterol** 51:144-152, 2016. **(IF=6.132)**

93. Miyata T, Kitano M, Omoto S, Kadosaka K, Kamata K, Imai H, Sakamoto H, Nishida N, Harwani Y, Murakami T, Takeyamas Y, Chiba Y, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for assessment of lymph node metastases in pancreatobiliary carcinoma. **World J Gastroenterol** 22:3381-3391, 2016. **(IF=3.665)**

94. Minami Y, Minami T, Chishina H, Kono M, Arizumi T, Takita M, Yada N, Hagiwara S, Ida H, Ueshima K, Nishida N, **Kudo M**: US-US fusion imaging in radiofrequency ablation for liver metastases. **Digest Dis** 34:687-691, 2016. **(IF=2.493)**

95. Makino Y, Imai Y, Igura T, Kogita S, Sawai Y, Fukuda K, Iwamoto T, Okabe J, Takamura M, Fujita N, Hori M, Takehara T, **Kudo M**, Murakami T: Feasibility of extracted-overlay fusion imaging for intraoperative treatment evaluation of radiofrequency ablation for hepatocellular carcinoma. **Liver Cancer** 5:269-279, 2016. **(IF=9.720)**

96. Minaga K, Kitano M, Yoshikawa T, Omoto S, Kamata K, Yamao K, **Kudo M**: Hepaticogastrostomy guided by real-time contrast-enhanced harmonic endoscopic ultrasonography: a novel technique. **Endoscopy** 48:E228-229, 2016. **(IF=7.341)**

97. Piscaglia F, **Kudo M**, Han KH, Sirlin C: Diagnosis of hepatocellular carcinoma with non-invasive imaging: a plea for worldwide adoption of standard and precise terminology for describing enhancement criteria. **Ultraschall Med** 38:9-11, 2017. **(IF=4.966)**

98. Kono M, Minami Y, Iwanishi M, Minami T, Chishina H, Arizumi T, Komeda Y, Sakurai T, Takita M, Yada N, Ida H, Hagiwara S, Ueshima K, Nishida N, **Kudo M***: Contrast-enhanced tissue harmonic imaging versus phase inversion harmonic sonographic imaging for the delineation of hepatocellular

carcinomas. **Oncology** 92:29-34, 2017. **(IF=2.642)**

99. Kamata K, Takenaka M, Minaga, **Kudo M**: Utility of contrast-enhanced harmonic EUS for evaluating the effects of steroid therapy in a case of IgG4-negative focal autoimmune pancreatitis. **Gastrointest Endosc** 86:1177-1179, 2017. **(IF=6.890)**

100. Minaga K, Takenaka M, Kamata K, Miyata T, Yamao K, Imai H, **Kudo M**: Endoscopic ultrasound-guided choledochoduodenostomy with novel use of contrast-enhanced harmonic imaging. **Endoscopy** 49:E281-E282, 2017. **(IF=7.341)**

101. Kamata K, Takenaka M, Kitano M, Omoto S, Miyata T, Minaga K, Yamao K, Imai H, Sakurai T, Watanabe T, Nishida N, Chikugo T, Chiba Y, Imamoto H, Yasuda T, Lisotti A, Fusaroli P, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for differential diagnosis of submucosal tumors of the upper gastrointestinal tract. **J Gastroenterol Hepatol** 32:1686-1692, 2017. **(IF=3.437)**

102. Minaga K, Takenaka M, Omoto S, Miyata T, Kamata K, Yamao K, Imai H, Watanabe T, Kitano M, **Kudo M**: A case of successful transluminal drainage of walled-off necrosis under contrast-enhanced harmonic endoscopic ultrasonography guidance. **J Med Ultrason** 45:161-165, 2018. **J Med Ultrason**

103. Kamata K, Takenaka M, Kitano M, Omoto S, Miyata T, Minaga K, Yamao K, Imai H, Sakurai T, Nishida N, Kashida H, Chikugo T, Chiba Y, Nakai T, Takeyama Y, Lisotti A, Fusaroli P, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for differential diagnosis of localized gallbladder lesions. **Dig Endosc** 30:98-106, 2018. **(IF=4.773)**

104. Minami Y, Minami T, Hagiwara S, Ida H, Ueshima K, Nishida N, Murakami T, **Kudo M**: Ultrasound-ultrasound image overlay fusion improves real-time control of radiofrequency ablation margin in the treatment of hepatocellular carcinoma. **Eur Radiol** 28:1986-1993, 2018. **(IF=4.101)**

105. Dietrich CF, Averkiou M, Nielsen MB, Barr RG, Burns PN, Calliada F, Cantisani V, Choi B, Chammas MC, Clevert DA, Claudon M, Correas JM, Cui XW, Cosgrove D, D'Onofrio M, Dong Y, Eisenbrey J, Fontanilla T, Gilja OH, Ignee A, Jenssen C, Kono Y, **Kudo M**, Lassau N, Lyshchik A, Franca Meloni M, Moriyasu F, Nolsøe C, Piscaglia F, Radzina M, Saftoiu A, Sidhu PS, Sporea I, Schreiber-Dietrich D, Sirlin CB, Stanczak M, Weskott HP, Wilson SR, Willmann JK, Kim TK, Jang HJ, Vezeridis A, Westerway S: How to perform contrast-enhanced ultrasound (CEUS). **Ultrasound Int Open** 4:E2-15, 2018. **(IF=0.000)**

106. Yamashita Y, Shimokawa T, Napoléon B, Fusaroli P, Gincul R, **Kudo M**, Kitano M: Value of contrast-enhanced harmonic EUS with enhancement pattern for diagnosis of pancreatic cancer: a meta-analysis. **Dig Endosc** 31:125-133, 2019. **(IF=4.774)**

107. **Kudo M***, Ueshima K, Osaki Y, Hirooka M, Imai Y, Aso K, Numata K, Kitano M, Kumada K, Izumi N, Sumino Y, Ogawa C, Akazawa K, for the SELECTED

Study Group, Japan: B-mode ultrasonography versus contrast-enhanced ultrasonography for surveillance of hepatocellular carcinoma: a prospective multicenter randomized controlled trial. **Liver Cancer** 8:271-280, 2019. **(IF=9.720)**

108. Tanaka H, Kamata K, Takenaka M, Yoshikawa T, Ishikawa R, Okamoto A, Yamazaki T, Nakai A, Omoto S, Minaga K, Yamao K, Sakurai T, Watanabe T, Nishida N, Chiba Y, Kitano M, **Kudo M**: Contrast-enhanced harmonic endoscopic ultrasonography for evaluating the response to chemotherapy in pancreatic cancer. **Dig Liver Dis** 51:1130-1134, 2019. **(IF=2.493)**

109. Morita M, Ogawa C, Omura A, Noda T, Kubo A Matsunaka T, Tamaki H, Shibatoge M, Seno H, Minami Y, Ueshima K, Sakurai T, Nishida N, **Kudo M***: The efficacy of Sonazoid-enhanced ultrasonography in decision-making for liver abscess treatment. **Intern Med** 59:471-477, 2020. **(IF=1.005)**

110. Minami Y, Minami T, Chishina H, Takita M, Hagiwara S, Ida H, Ueshima K, Nishida N, **Kudo M***: Radiofrequency ablation for hepatocellular carcinoma: clinical value of ultrasound-u-ltrasound overlay fusion for optimal ablation and local controllability. **Hepatol Res** 50:67-74, 2020. **(IF=3.165)**

111. Minami Y, **Kudo M**: Ultrasound fusion imaging technologies for guidance in ablation therapy for liver cancer. **J Med Ultrasoun** 47:257-263, 2020. **(IF=0.000)**

112. Lee JY, Minami Y, Choi BI, Lee WJ, Chou YH, Jeong WK, Park MS, Kudo N, Lee MW, Kamata K, Iijima H, Kim SY, Numata K, Sugimoto K, Maruyama H, Sumino Y, Ogawa C, Kitano M, Joo I, Arita J, Liang JD, Lin HM, Nolsoe C, Gilja OH, **Kudo M**: The AFSUMB consensus statements and recommendations for the clinical practice of contrast-enhanced ultrasound using sonazoid. **Ultrasonography**, 2020 (Epub ahead of print). **(IF=3.075)**

113. Dietrich CF, Nolsoe CP, Barr RG, Berzigotti A, Bums PN, Cantisani V, Chammas MC, Caubal N, Choi BI, Clevert DA, Cui X, Dong Y, D'Onofrio M, Fowlkes JB, Gilja OH, Huang P, Ignee A, Jenssen C, Kono Y, **Kudo M**, Lassau N, Lee WJ, Lee JY, Liang P, Lim A, Lyshchik A, Meloni MF, Correas JM, Minami Y, Moriyasu F, Nicolau C, Piscaglia F, Saftoiu A, Sidhu PS, Sporea I, Torzilli G, Xie X, Zheng R: Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver-update 2012: a WFUMB ub cooperation with EFSUMB, AFSUMB, AIUM, and FLAUS. **Ultrasound Med Biol** 2020 (Epub ahead of print). **(IF=2.514)**

114. Dietrich CF, Nolsoe CP, Barr RG, Berzigotti A, Bums PN, Cantisani V, Chammas MC, Caubal N, Choi BI, Clevert DA, Cui X, Dong Y, D'Onofrio M, Fowlkes JB, Gilja OH, Huang P, Ignee A, Jenssen C, Kono Y, **Kudo M**, Lassau N, Lee WJ, Lee JY, Liang P, Lim A, Lyshchik A, Meloni MF, Correas JM, Minami Y, Moriyasu F, Nicolau C, Piscaglia F, Saftoiu A, Sidhu PS, Sporea I, Torzilli G, Xie X, Zheng R: Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver-update 2012: a WFUMB ub cooperation with EFSUMB, AFSUMB, AIUM, and FLAUS. **Ultraschall in Med** 2020 (Epub ahead of print). **(IF=4.966)**