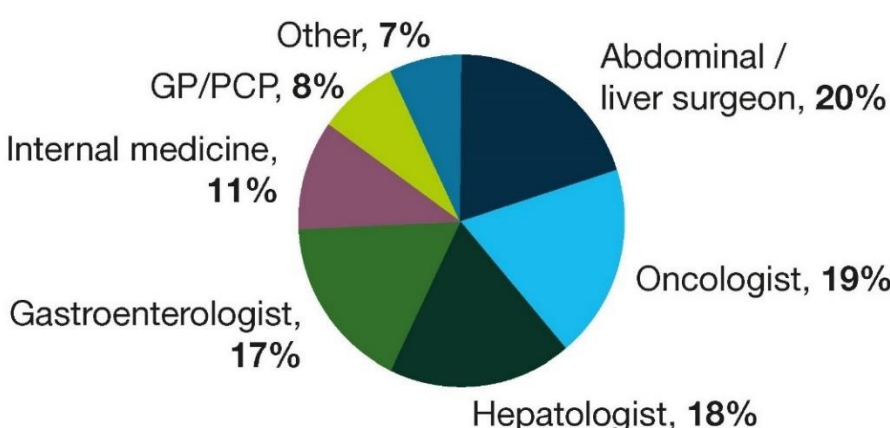
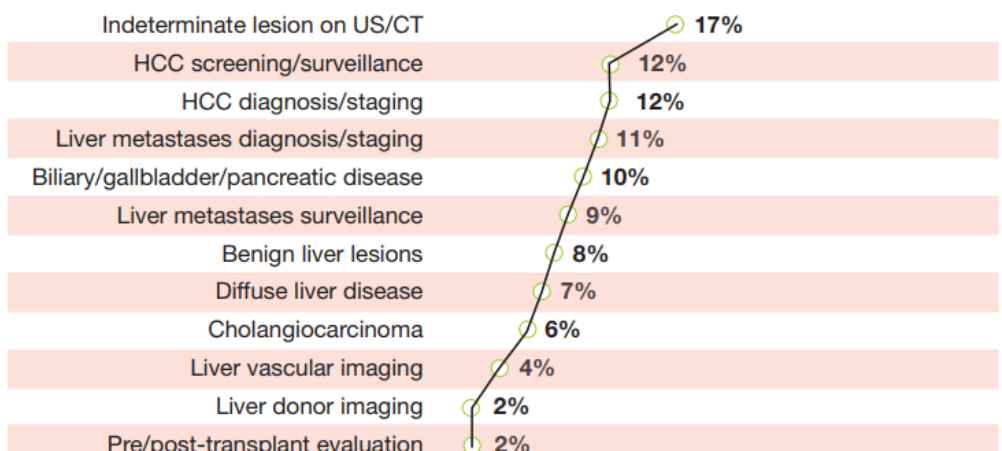


**Consensus report from the 10th Global Forum for Liver Magnetic Resonance
Imaging: developments in HCC management**

Electronic Supplementary Material

Questionnaire survey results: global survey on gadoxetic acid usage

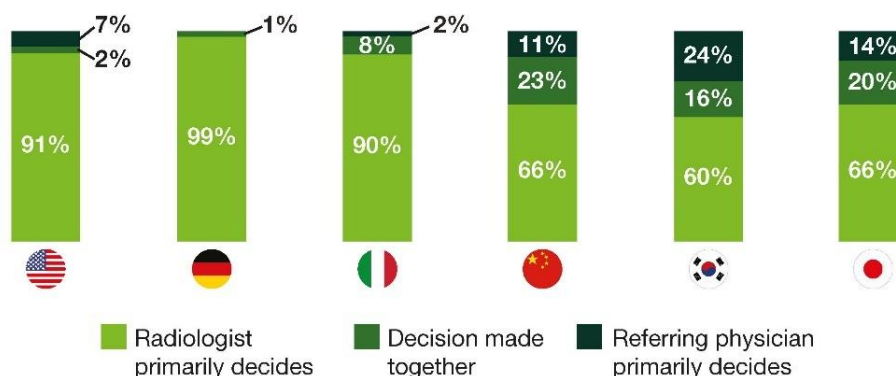
A survey developed by Professor Taouli and a Bayer research team was completed by 453 radiologists from China, Germany, Italy, Japan, South Korea, and USA in advance of the 10th Global Liver Forum to explore current practice in liver MRI. Professor Taouli presented and commented on the survey results at the Forum.

<p>Survey methodology</p> <p>The survey was a quantitative, double-blinded 25-minute online questionnaire performed between August 2021 and December 2021 by specialized/board radiologists who had been certified for at least 3 years and fewer than 35 years. The participants were from China ($n = 101$), Germany ($n = 80$), Italy ($n = 52$), Japan ($n = 70$), South Korea ($n = 50$), and USA ($n = 110$).</p>																											
<p>Referrals for imaging</p> <p>Referrals for liver imaging (CT or MRI) came almost equally from abdominal/liver surgeons, oncologists, hepatologists, and gastroenterologists, with the remainder from internal medicine physicians, general practitioners (GP)/primary care physicians (PCP), and other.</p>	<p>Referrals for liver imaging come almost equally from surgeons, oncologists, hepatologists, and gastroenterologists</p>  <table border="1"> <thead> <tr> <th>Specialty</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>Abdominal / liver surgeon</td> <td>20%</td> </tr> <tr> <td>Oncologist</td> <td>19%</td> </tr> <tr> <td>Hepatologist</td> <td>18%</td> </tr> <tr> <td>Gastroenterologist</td> <td>17%</td> </tr> <tr> <td>Internal medicine</td> <td>11%</td> </tr> <tr> <td>GP/PCP</td> <td>8%</td> </tr> <tr> <td>Other</td> <td>7%</td> </tr> </tbody> </table>	Specialty	Percentage	Abdominal / liver surgeon	20%	Oncologist	19%	Hepatologist	18%	Gastroenterologist	17%	Internal medicine	11%	GP/PCP	8%	Other	7%										
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<p>The most common reasons for referrals for liver MRI were indeterminate lesions on US or CT, HCC screening/surveillance, HCC diagnosis/staging, liver metastases diagnosis and staging, and diseases of the biliary system or pancreatic disease.</p>	<p>Indications for liver MRI</p> <p>Most frequent: indeterminate lesion on US/CT</p>  <table border="1"> <thead> <tr> <th>Indication</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>Indeterminate lesion on US/CT</td> <td>17%</td> </tr> <tr> <td>HCC screening/surveillance</td> <td>12%</td> </tr> <tr> <td>HCC diagnosis/staging</td> <td>12%</td> </tr> <tr> <td>Liver metastases diagnosis/staging</td> <td>11%</td> </tr> <tr> <td>Biliary/gallbladder/pancreatic disease</td> <td>10%</td> </tr> <tr> <td>Liver metastases surveillance</td> <td>9%</td> </tr> <tr> <td>Benign liver lesions</td> <td>8%</td> </tr> <tr> <td>Diffuse liver disease</td> <td>7%</td> </tr> <tr> <td>Cholangiocarcinoma</td> <td>6%</td> </tr> <tr> <td>Liver vascular imaging</td> <td>4%</td> </tr> <tr> <td>Liver donor imaging</td> <td>2%</td> </tr> <tr> <td>Pre/post-transplant evaluation</td> <td>2%</td> </tr> </tbody> </table>	Indication	Percentage	Indeterminate lesion on US/CT	17%	HCC screening/surveillance	12%	HCC diagnosis/staging	12%	Liver metastases diagnosis/staging	11%	Biliary/gallbladder/pancreatic disease	10%	Liver metastases surveillance	9%	Benign liver lesions	8%	Diffuse liver disease	7%	Cholangiocarcinoma	6%	Liver vascular imaging	4%	Liver donor imaging	2%	Pre/post-transplant evaluation	2%
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MRI contrast agent choice

In the majority of countries, with some variation, the radiologist primarily decides which contrast agent is injected into the patient: up to 99% in Germany, 91% in USA, and slightly less in South Korea, where there is also a decision made by the referring physician.

Decisions regarding choice of contrast agent largely lie with radiologists



Liver imaging practice

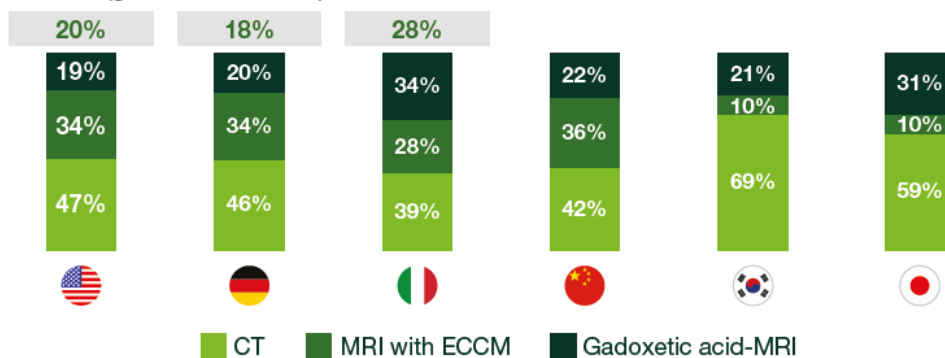
In most countries, CT is still the predominant liver imaging modality, as expected: from 69% in South Korea to as low as 39% in Italy, but ~40–70% of cases overall.

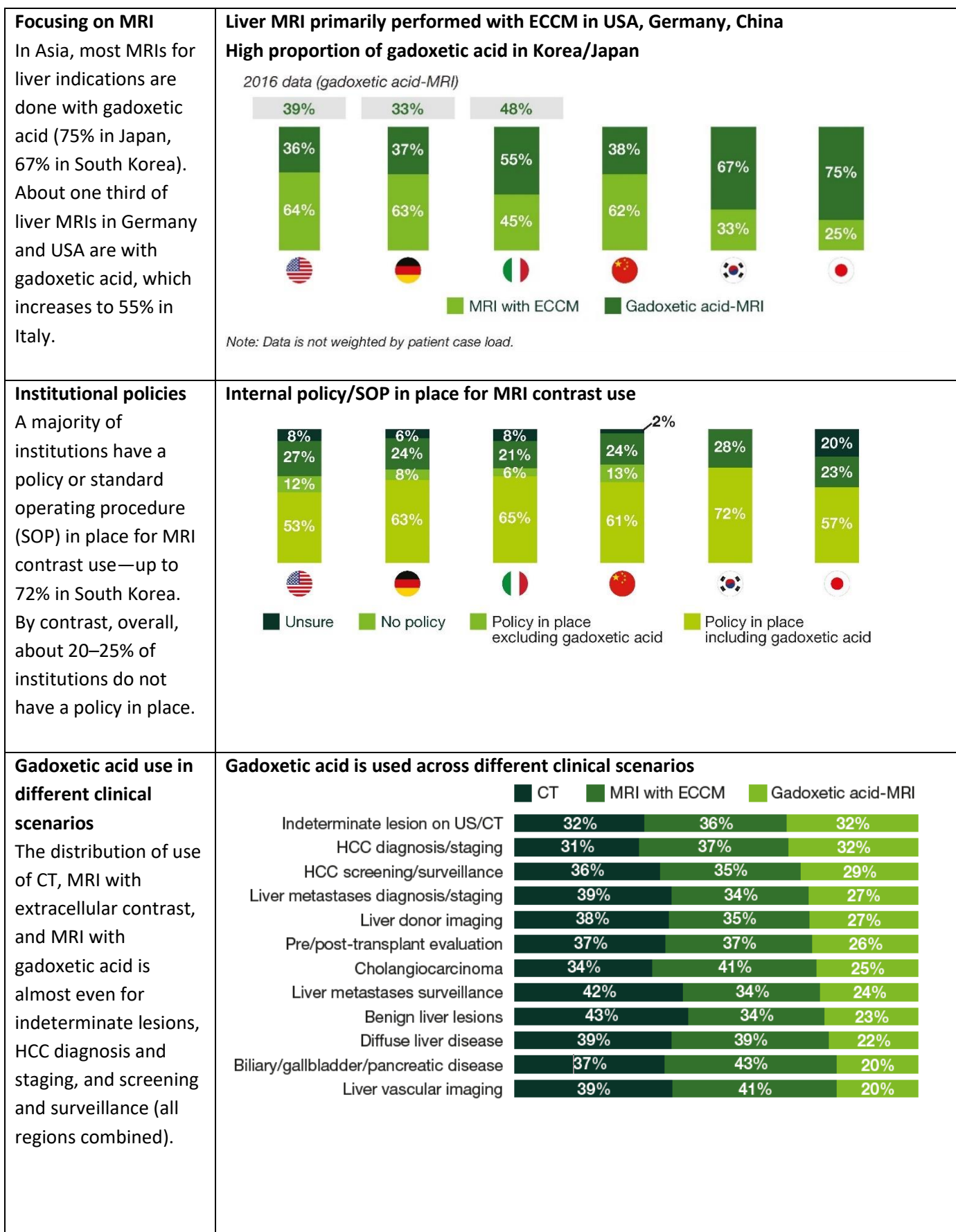
For MRI, there are a large proportion of images with ECCM and a smaller proportion (about 19–34%) with gadoxetic acid-MRI. Data from a 2016 survey of radiologists in Germany, Italy, and USA show there has been minimal change in the use of gadoxetic acid.

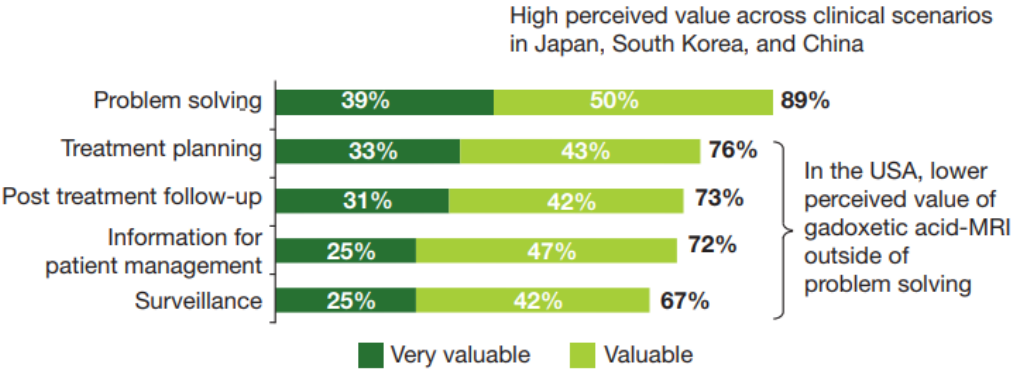
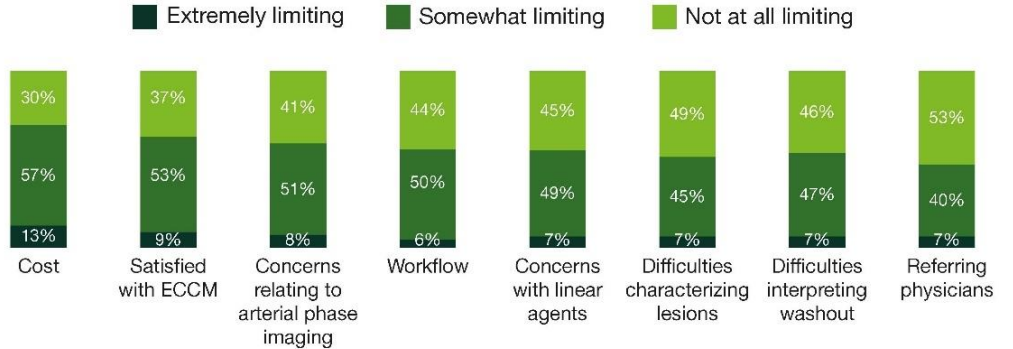
Liver imaging practice differs by country

Korea/Japan: high use of CT and a preference for gadoxetic acid for MRI

2016 data (gadoxetic acid-MRI)











<p>Perceived value of gadoxetic acid-enhanced MRI</p> <p>Gadoxetic-enhanced MRI was perceived as valuable or very valuable for problem solving, treatment planning, and treatment follow-up—whether for HCC or metastases.</p>	<p>Gadoxetic acid-MRI is most valuable for problem solving</p> <p>High perceived value across clinical scenarios in Japan, South Korea, and China</p>  <table border="1"> <thead> <tr> <th>Clinical Scenario</th> <th>Very valuable (%)</th> <th>Valuable (%)</th> <th>Total (%)</th> </tr> </thead> <tbody> <tr> <td>Problem solving</td> <td>39%</td> <td>50%</td> <td>89%</td> </tr> <tr> <td>Treatment planning</td> <td>33%</td> <td>43%</td> <td>76%</td> </tr> <tr> <td>Post treatment follow-up</td> <td>31%</td> <td>42%</td> <td>73%</td> </tr> <tr> <td>Information for patient management</td> <td>25%</td> <td>47%</td> <td>72%</td> </tr> <tr> <td>Surveillance</td> <td>25%</td> <td>42%</td> <td>67%</td> </tr> </tbody> </table> <p>In the USA, lower perceived value of gadoxetic acid-MRI outside of problem solving</p>	Clinical Scenario	Very valuable (%)	Valuable (%)	Total (%)	Problem solving	39%	50%	89%	Treatment planning	33%	43%	76%	Post treatment follow-up	31%	42%	73%	Information for patient management	25%	47%	72%	Surveillance	25%	42%	67%												
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<p>Barriers to gadoxetic acid use</p> <p>The top reason for not using gadoxetic acid was cost, which applied to most countries. Radiologists were also satisfied with extracellular agents, which were incorporated into standardized reporting protocols. Another issue was arterial phase imaging with gadoxetic acid. Finally, there were other issues with workflow, difficulty interpreting washout, etc.</p>	<p>Barriers for gadoxetic acid use</p>  <table border="1"> <thead> <tr> <th>Barrier</th> <th>Extremely limiting (%)</th> <th>Somewhat limiting (%)</th> <th>Not at all limiting (%)</th> </tr> </thead> <tbody> <tr> <td>Cost</td> <td>13%</td> <td>57%</td> <td>30%</td> </tr> <tr> <td>Satisfied with ECCM</td> <td>9%</td> <td>53%</td> <td>37%</td> </tr> <tr> <td>Concerns relating to arterial phase imaging</td> <td>8%</td> <td>51%</td> <td>41%</td> </tr> <tr> <td>Workflow</td> <td>6%</td> <td>50%</td> <td>44%</td> </tr> <tr> <td>Concerns with linear agents</td> <td>7%</td> <td>49%</td> <td>45%</td> </tr> <tr> <td>Difficulties characterizing lesions</td> <td>7%</td> <td>45%</td> <td>49%</td> </tr> <tr> <td>Difficulties interpreting washout</td> <td>7%</td> <td>47%</td> <td>46%</td> </tr> <tr> <td>Referring physicians</td> <td>7%</td> <td>40%</td> <td>53%</td> </tr> </tbody> </table> <p>In 2016 research, workflow was identified as the 2nd most important barrier. With new codes added, this now is the 4th most important barrier.</p>	Barrier	Extremely limiting (%)	Somewhat limiting (%)	Not at all limiting (%)	Cost	13%	57%	30%	Satisfied with ECCM	9%	53%	37%	Concerns relating to arterial phase imaging	8%	51%	41%	Workflow	6%	50%	44%	Concerns with linear agents	7%	49%	45%	Difficulties characterizing lesions	7%	45%	49%	Difficulties interpreting washout	7%	47%	46%	Referring physicians	7%	40%	53%
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Survey results showed that the LiRADS group has gained widespread acceptance—globally around 78%. In Japan, 90% of surveyed radiologists were using local guidelines from the Japanese Society of Hepatology and only 32% were using LiRADS. Interestingly, the United States Organ Procurement and Transplantation Network (OPTN) guidance was used by 20% of surveyed radiologists in China.

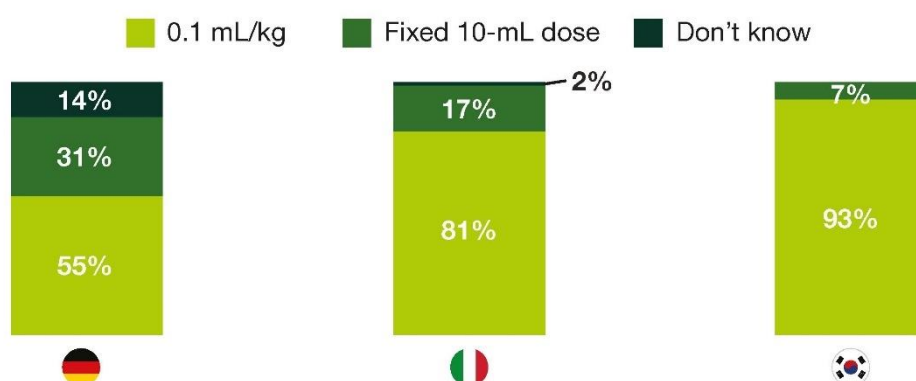
LiRADS is the most commonly used classification system for HCC (except Japan/Korea)

% radiologists using each of the following classification systems	LiRADS	OPTN	EASL	APASL	JSH	Korean Guidelines
Global	78%	11%	24%	22%	14%	5%
	95%	7%	4%	0%		
	63%	4%	35%	3%		
	71%	4%	44%	8%		
	87%	20%	45%	48%		
	66%	0%	0%	2%		98%
	33%	3%	7%	7%	90%	

Gadoxetic acid dosing

There was variation in the dosing used: some radiologists used a fixed dose of 10 mL (related to the desire to avoid waste), but ~55–93% of surveyed radiologists were using a Food and Drug Administration- or European Medicines Agency-approved dose of 0.1 mL/kg (radiologists from Japan and USA were not surveyed).

Weight-based dosing is most common



<p>Protocol for arterial phase imaging</p> <p>The protocol used for arterial phase imaging with gadoxetic acid also showed regional variation. The top three methods were: fixed delay, a test bolus for arterial phase timing, or fluoroscopic triggering/automated bolus detection algorithm.</p>	<p>Arterial phase timing techniques for gadoxetic acid</p> <p>Arterial phase timing techniques used (% radiologists using each most frequently) Base: gadoxetic acid users, $n = 412$</p> <table border="1"> <thead> <tr> <th>Technique</th> <th>USA</th> <th>Germany</th> <th>Italy</th> <th>China</th> <th>South Korea</th> <th>Japan</th> </tr> </thead> <tbody> <tr> <td>Fixed delay</td> <td>37%</td> <td>24%</td> <td>17%</td> <td>24%</td> <td>22%</td> <td>19%</td> </tr> <tr> <td>Test bolus timing</td> <td>23%</td> <td>27%</td> <td>29%</td> <td>17%</td> <td>54%</td> <td>34%</td> </tr> <tr> <td>Fluoroscopic triggering / automated bolus detection algorithm</td> <td>13%</td> <td>11%</td> <td>40%</td> <td>32%</td> <td>10%</td> <td>29%</td> </tr> <tr> <td>Time-resolved imaging</td> <td>16%</td> <td>30%</td> <td>8%</td> <td>22%</td> <td>2%</td> <td>-</td> </tr> <tr> <td>Don't know</td> <td>9%</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p>Most commonly referenced arterial phase timing techniques</p>	Technique	USA	Germany	Italy	China	South Korea	Japan	Fixed delay	37%	24%	17%	24%	22%	19%	Test bolus timing	23%	27%	29%	17%	54%	34%	Fluoroscopic triggering / automated bolus detection algorithm	13%	11%	40%	32%	10%	29%	Time-resolved imaging	16%	30%	8%	22%	2%	-	Don't know	9%					
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<p>Vendors used by the radiologists</p> <p>Globally, about half the surveyed radiologists were using a Siemens scanner, followed by GE, then Philips. Field strength was basically equal between 3T and 1.5T.</p>	<p>Scanner vendors and field strengths for gadoxetic acid-MRI</p> <p>Vendors % radiologists using each for gadoxetic acid-MRI Base: gadoxetic acid users, $n = 412$</p> <table border="1"> <thead> <tr> <th>Vendor</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>Siemens</td> <td>51%</td> </tr> <tr> <td>GE</td> <td>39%</td> </tr> <tr> <td>Philips</td> <td>32%</td> </tr> <tr> <td>Canon/Toshiba</td> <td>4%</td> </tr> <tr> <td>Fujifilm/Hitachi (Japan only)</td> <td>3%</td> </tr> </tbody> </table> <p>Field strength % radiologists using each for gadoxetic acid-MRI Base: gadoxetic acid users, $n = 412$</p> <table border="1"> <thead> <tr> <th>Field strength</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>3 T</td> <td>63%</td> </tr> <tr> <td>1.5 T</td> <td>60%</td> </tr> <tr> <td>0.55 T</td> <td>3%</td> </tr> <tr> <td>0.5 T</td> <td>1%</td> </tr> <tr> <td>7 T</td> <td>1%</td> </tr> </tbody> </table> <p>Greater in South Korea (95%) Greater in Italy (94%)</p>	Vendor	%	Siemens	51%	GE	39%	Philips	32%	Canon/Toshiba	4%	Fujifilm/Hitachi (Japan only)	3%	Field strength	%	3 T	63%	1.5 T	60%	0.55 T	3%	0.5 T	1%	7 T	1%																		
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<p>The scenarios for using abbreviated protocols with gadoxetic acid varied. The top indication was initial diagnosis of liver metastases, which is an interesting finding. We assume that HCC diagnosis is an additional use of the abbreviated protocol, but we did not ask that question.</p>	<p>Abbreviated protocols are used across different clinical scenarios</p> <p>Clinical scenarios where abbreviated protocols are used (% radiologists selection each) Base: radiologists using abbreviated protocols (n = 123)</p> <table border="1"> <thead> <tr> <th>Clinical Scenario</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>Initial diagnosis of liver metastases</td> <td>68%</td> </tr> <tr> <td>HCC screening</td> <td>56%</td> </tr> <tr> <td>HCC follow-up</td> <td>55%</td> </tr> <tr> <td>Liver metastases follow-up</td> <td>48%</td> </tr> <tr> <td>Other</td> <td>3%</td> </tr> </tbody> </table> <p><i>Single mentions: FNH assessment, differential diagnosis of liver lesion, dynamic enforcement</i></p>	Clinical Scenario	Percentage	Initial diagnosis of liver metastases	68%	HCC screening	56%	HCC follow-up	55%	Liver metastases follow-up	48%	Other	3%
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<p>Summary of survey outcomes</p> <ul style="list-style-type: none"> • Gadoxetic acid versus ECCM use is stable/minimally increased in USA/Europe. • Gadoxetic acid is used in 19–34% of cases. • Gadoxetic acid is used more often than ECCM in Asia. • Most radiologists viewed gadoxetic acid as a problem-solving agent. • Most radiology centers have contrast guidelines that reference gadoxetic acid. • Barriers to gadoxetic acid use are cost and satisfaction with ECCM. • There is a potential role for abbreviated MRI using gadoxetic acid. 													