Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2025-B-354-z Gadopiclenol

Stand: Februar 2026

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Gadopiclenol **Diagnostikum zur MRT-Kontrastverstärkung (Alter 0 bis 2 Jahre)**	
Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet".
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	nicht angezeigt
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Beschluss über die Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V für den Wirkstoff Gadopiclenol vom 19. September 2024 (Alter ab 2 Jahren).
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	Siehe systematische Literaturrecherche

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff ATC-Code Handelsname	Anwendungsgebiet (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Gadopiclenol V08CA12 Elucirem, Vueway	<u>Anwendungsgebiet laut positive opinion:</u> This medicinal product is for diagnostic use only. Gadopiclenol is indicated in adults and children **from birth** ~~aged 2 years and older~~ for contrastenhanced magnetic resonance imaging (MRI) to improve detection and visualization of pathologies with disruption of the bloodbrainbarrier (BBB) and/or abnormal vascularity of: - the brain, spine, and associated tissues of the central nervous system (CNS); - the liver, kidney, pancreas, breast, lung, prostate, and musculoskeletal system. It should be used only when diagnostic information is essential and not available with unenhanced MRI."
Paramagnetische MRT-Kontrastmittel	
Gadotersäure V08CA02 generisch	Dieses Arzneimittel ist ein Diagnostikum. Clariscan™ sollte nur dann angewendet werden, wenn die diagnostische Information notwendig ist und mit einer Magnetresonanztomographie (MRT) ohne Kontrastmittelverstärkung nicht erhoben werden kann. Clariscan™ ist ein Kontrastmittel zur Kontrastverstärkung bei der Magnetresonanztomographie (MRT) und damit zur besseren Darstellung bzw. Abgrenzung <u>Erwachsene, Kinder und Jugendliche (0 – 18 Jahre):</u> – Läsionen des Gehirns, des Rückenmarks und des umgebenden Gewebes – Ganzkörper-MRT (s. Abschnitt 4.2) Die Anwendung zur Ganzkörper-MRT wird bei Kindern unter 6 Monaten nicht empfohlen. <u>Nur bei Erwachsenen:</u> – Läsionen oder Stenosen der nicht-koronaren Arterien (MR-Angiographie). *[Stand FI Clariscan 05/2024]*
Gadoteridol V08CA04 ProHance	Dieses Arzneimittel ist ein Diagnostikum. ProHance ist ein nichtionisches paramagnetisches Kontrastmittel zur Magnetresonanz-Tomographie (MRT). Beim Einsatz in der MRT ermöglicht ProHance eine Kontrastverstärkung – des Gehirns, des Rückenmarks und des umgebenden Gewebes mit verbesserter Darstellung (im Vergleich zur nicht kontrastverstärkten MRT) von Läsionen mit abnormer Vaskularität oder Läsionen, die eine Störung der Blut-Hirn-Schranke verursachen können: – von Weichteiltumoren im Kopf- und Halsbereich – des muskuloskelettalen Systems von Körperstamm und Extremitäten – bei Erkrankungen der Brust

	– bei der Differentialdiagnose von Lebertumoren – bei Erkrankungen im Beckenbereich. ProHance sollte nur dann angewendet werden, wenn die diagnostische Information notwendig ist und mit einer Magnetresonanztomographie (MRT) ohne Kontrastmittelverstärkung nicht erhoben werden kann. ProHance wird angewendet bei Erwachsenen, Kindern und Jugendlichen ab der Geburt. Die Anwendung einer Ganzkörper-MRT wird bei Patienten unter 18 Jahren nicht empfohlen. *[Stand FI 08/2024]*
Gabobensäure V08CA08 MultiHance	Dieses Arzneimittel ist ein Diagnostikum. MultiHance ist ein paramagnetisches Kontrastmittel zur Magnetresonanztomografie (MRT) **der Leber** bei Erwachsenen und Kindern (ab 2 Jahren). MultiHance sollte nur dann angewendet werden, wenn die diagnostische Information notwendig ist und mit einer Magnetresonanztomografie (MRT) ohne Kontrastmittelverstärkung nicht erhoben werden kann und eine Bildgebung der Spätphase erforderlich ist. *[Stand FI 05/2024]*
Gadobutrol V08CA09 Gadovist	Dieses Arzneimittel ist ein Diagnostikum. Gadovist ist indiziert für Erwachsene und Kinder jeden Alters (inklusive reifer Neugeborener) zur: • Kontrastverstärkung bei der kranialen und spinalen Magnetresonanztomographie (MRT). • Kontrastverstärkten MRT der Leber oder Nieren bei Patienten mit nachgewiesenen fokalen Läsionen oder bei dringendem Verdacht auf solche, um diese als benigne oder maligne zu klassifizieren. • Kontrastverstärkung bei der Magnetresonanzangiographie (CE-MRA). Gadovist kann auch für bildgebende MR-Untersuchungen pathologischer Strukturen im gesamten Körper eingesetzt werden. Es erleichtert die Visualisierung abnormaler Strukturen oder Läsionen und ermöglicht die Differenzierung zwischen gesundem und pathologischem Gewebe. Gadovist sollte nur dann angewendet werden, wenn die diagnostische Information notwendig ist und mit einer Magnetresonanztomographie (MRT) ohne Kontrastmittelverstärkung nicht erhoben werden kann. *[Stand FI Gadovist 09/2024]*
Gadoxetsäure V08CA10 Primovist	Primovist wird zur **Erkennung von fokalen Leberläsionen** eingesetzt und liefert Informationen über den Charakter dieser Läsionen mittels T1-gewichteter Magnetresonanztomographie (MRT). Primovist sollte nur dann angewendet werden, wenn die diagnostische Information notwendig ist und mit einer Magnetresonanztomographie (MRT) ohne Kontrastmittelverstärkung nicht erhoben werden kann und eine Bildgebung der Spätphase erforderlich ist. Dieses Arzneimittel ist ein Diagnostikum zur intravenösen Applikation. *[Stand FI 10/2024]*

Quellen: AMIce-Datenbank, Fachinformationen

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie

Vorgang: 2025-B-354z (Beratung nach § 35a SGB V) Gadoquatran

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	12. Januar 2026

Inhaltsverzeichnis

Abkürzungsverzeichnis

AKI	acute kidney injury
AUC	Area under the curve
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
BCLC	Barcelona Clinic Liver Cancer
ceMR	Contrast-enhanced magnetic resonance imaging
CIEDs	Cardiac implantable electronic devices
DCE	Dynamic contrast enhanced
DSA	Digital subtraction angiography
DSC	Dynamic susceptibility contrast
DWI	Diffusion weighted imaging
ECA	Extracellular contrast agent
ECRI	Emergency Care Research Institute
eGFR	estimated glomerular filtration rate
EOB	Hepatobiliary agent
G-BA	Gemeinsamer Bundesausschuss
GBCA	gadolinium-based contrast agent
GIN	Guidelines International Network
GoR	Grade of Recommendations
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBP	Hepatobiliary phase
HCC	Hepatocellular carcinoma
HR	Hazard Ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LI-RADS	Liver Reporting and Data System
LoE	Level of Evidence
LRT	Locoregional therapies
MR	Magnetic resonance
MRS	Magnetic resonance spectroscopy
NICE	National Institute for Health and Care Excellence
NSF	nephrogenic systemic fibrosis
OR	Odds Ratio
RFA	Radiofrequency ablation
RR	Relatives Risiko

SIGN   Scottish Intercollegiate Guidelines Network

TACE   Transarterial chemoembolization

TRIP   Turn Research into Practice Database

WHO   World Health Organization

1 Indikation

In adults and children from birth aged 2 years and older for contrast-enhanced magnetic resonance imaging (MRI) to improve detection and visualization of pathologies with disruption of the blood-brain-barrier (BBB) and/or abnormal vascularity of:

- the brain, spine, and associated tissues of the central nervous system (CNS);

- the liver, kidney, pancreas, breast, lung, prostate, and musculoskeletal system.

Hinweis zur Synopse: Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation Kontrastverstärkung bei MRT-Bildgebung durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinien-organisationen. Ergänzend wurde eine freie Internetsuche (*https://www.google.com/*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum der systematischen Literaturrecherche wurde auf die letzten fünf Jahre eingeschränkt und die Recherchen am 07.01.2026 abgeschlossen. Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Auflistung durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherchen ergaben insgesamt 1684 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Dabei wurde für systematische Reviews, inkl. Meta-Analysen, ein Publikationszeitraum von 2 Jahren und für Leitlinien von 5 Jahren betrachtet. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen als Volltexte gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet. Basierend darauf, wurden insgesamt 3 Referenzen eingeschlossen. Es erfolgt eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine relevanten CR identifiziert.

3.2 Systematische Reviews

Zhou S et al., 2024 [3].

Diagnostic performance of MRI for residual or recurrent hepatocellular carcinoma after locoregional treatment according to contrast agent type: a systematic review and meta-analysis

Fragestellung

The ideal contrast agent for imaging patients with hepatocellular carcinoma (HCC) following locoregional therapies (LRT) remains uncertain. We conducted a meta-analysis to assess the diagnostic performance of magnetic resonance imaging with extracellular contrast agent (ECA-MRI) and hepatobiliary agent (EOB-MRI) in detecting residual or recurrence HCC following LRT.

Methodik

Population:

- HCC patients underwent LRT, encompassing TACE (conventional-TACE / drug-eluting bead-TACE) or ablations (radiofrequency ablation/microwave ablation);

Intervention/Komparator:

- ECAMRI or EOB-MRI were performed after LRT

Endpunkte:

- sensitivity and specificity of ECA-MRI and EOB-MRI in detecting residual or recurrent HCC after LRT. The secondary outcomes included assessment of factors influencing variability in diagnostic performance, including patient characteristics, types of LRT employed, and risk of bias.

Recherche/Suchzeitraum:

- PubMed MEDLINE, EMBASE, Cochrane Library and Web of Science databases
- Zeitraum NA

Qualitätsbewertung der Studien:

- Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool [15] was used to assess the quality of the selected studies.

Ergebnisse

Anzahl eingeschlossener Studien:

- 15
- 803 patients and 1018 lesions
- 10 studies used ECA-MRI only, three studies used EOB-MRI only, and two studies directly compared the diagnostic performance of ECA-MRI and EOB-MRI for HCC response after

LRT (Rimola et.al reported the outcomes of radiofrequency ablation (RFA) and TACE respectively)

Charakteristika der Population/Studien:

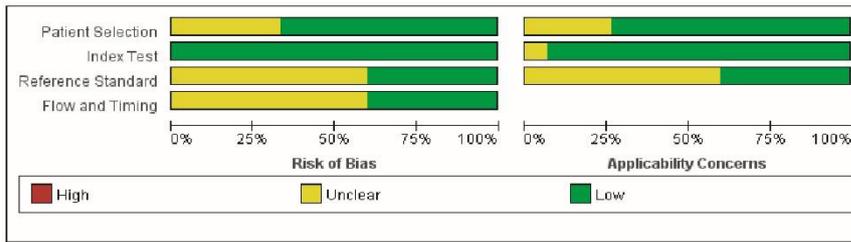**Table 1** Characteristics of the included studies

Author, Year (References)	Country	Study design	Study period	Locoregional treatment	No. of patients	Male/Female	Age (median) (Range)	Most common etiology of liver disease (number)	No. of lesions (No. of HCC)	Mean size (cm)	Gold standard	Time of post-treated examination	Field strength (Tesla)	Contrast agent	Blind
Goshima et al., 2008 [19]	Japan	Retro	NR	C-TACE	25	18 / 7	60 (mean) (48–79)	HCV (22)	39 (14)	NR	Fu	2–6 months	1.5	ECA	Y
Bolog et al., 2008 [18]	Switzerland	Retro	2001.07–2004.06	TACE	22	16 / 6	58 (mean) (24–74)	HCV (9)	30 (22)	3.11	Pathology/DSA	≤1 month	1.5	ECA	Y
Jin et al., 2008 [20]	China	Pro	2006.12–2007.05	C-TACE	48	37 / 11	43(mean) (27–78)	NR	92 (72)	5.1	DSA	1–2 months	3.0	ECA	Y
Yu et al., 2009 [21]	Korea	Retro	2007.04–2007.12	TACE	32	25 / 7	58 (mean) (35–75)	HBV (20)	36 (26)	NR	Fu/DSA	NR	1.5	ECA	NR
Kalb et al., 2010 [22]	USA	Pro	2005.12–2008.01	DEB-TACE/C-TACE	21	17 / 4	61 (mean) (51–78)	HCV (15)	23 (7)	3.4	Pathology/Fu	≤1 month	1.5	ECA	Y
Osama et al., 2013 [23]	Egypt	Retro	2011.06–2012.12	C-TACE	50	42 / 8	60 (40–79)	NR	50 (21)	3.6	Fu/DSA	NR	1.5	ECA	NR
Ebeed et al., 2017 [24]	Egypt	Retro	2015.12–2016.11	TACE	30	24 / 6	59 (41–76)	NR	40 (17)	4.1	Fu	≤1 month	1.5	ECA	NR
Rimola-1 et al., 2019 [10]	USA	Retro	2005.01–2012.04	TACE	14	NR	NR	NR	19 (10)	NR	Pathology	NR	1.5 / 3.0	ECA	Y
Rimola-2 et al., 2019 [10]	USA	Retro	2005.01–2012.04	RFA	12	NR	NR	NR	17 (7)	NR	Pathology	NR	1.5 / 3.0	ECA	Y
Saleh et al., 2019 [25]	Egypt	Pro	NR	TACE	30	28/2	63 (mean) (49–72)	NR	40 (19)	3.12	Fu/DSA	≤1 month	3.0	ECA	NR
Yim et al., 2019 [11]	Korea	Retro	2015.11–2017.11	TACE/RFA/Resection	135	108/27	NR (32–76)	HBV (95)	136 (121)	1.9	Pathology/Fu	≤1 month	3.0	ECA	Y
Chaudhry et al., 2020 [26]	USA	Retro	2011.01–2015.12	Ablation	36	32 / 4	58 (mean) (NR)	HCV (20)	53 (22)	2.3	Pathology	NR	1.5 / 3.0	ECA	Y
Ahmed et al., 2022 [27]	Egypt	Retro	2020.09–2021.07	DEB-TACE / RFA/MWA	54	47 / 7	64 (23–77)	HCV (50)	81 (31)	NR	Pathology/Fu	≤1 month	1.5	ECA	Y
Watanabe et al., 2012 [28]	Japan	Pro	NR	RFA	42	26 / 16	71 (mean) (50–89)	HCV (34)	61 (10)	1.6	Fu	155 days	3.0	EOB	Y

Table 1 (continued)

Author, Year (References)	Country	Study design	Study period	Locoregional treatment	No. of patients	Male/Female	Age (median) (Range)	Most common etiology of liver disease (number)	No. of lesions (No. of HCC)	Mean size (cm)	Gold standard	Time of post-treated examination	Field strength (Tesla)	Contrast agent	Blind
Rimola-1 et al., 2019 [10]	Spain	Retro	2005.01–2012.04	TACE	10	NR	NR	NR	19 (7)	NR	Pathology	NR	1.5 / 3.0	EOB	Y
Rimola-2 et al., 2019 [10]	Spain	Retro	2005.01–2012.04	RFA	11	NR	NR	NR	19 (4)	NR	Pathology	NR	1.5 / 3.0	EOB	Y
Yim et al., 2019 [11]	Korea	Retro	2015.11–2017.11	TACE / RFA	135	108 / 27	NR (32–76)	HBV (95)	136 (121)	1.9	Pathology/Fu	≤1 month	3.0	EOB	Y
Rimola et al., 2020 [29]	Spain	Pro	2014.06–2017.12	Ablation/Resection	34	27 / 7	67 (63–73)	HCV (25)	53 (42)	1.2	Pathology/Fu	NR	1.5	EOB	Y
Liu et al., 2021 [30]	China	Retro	2018.01–2019.12	DEB-TACE	62	50 / 12	57 (mean) (32–79)	HBV (50)	74 (33)	3.4	Pathology/DSA	1–2 months	3.0	EOB	Y

NR not recorded, *Pro* prospective, *Retro* retrospective, *TACE* transarterial chemoembolization, *RFA* radiofrequency ablation, *MWA* microwave ablation, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *Fu* follow up, *DSA* digital subtraction angiography, *ECA* extracellular contrast agent, *EOB* hepatobiliary contrast agent, *Y* yes

Qualität der Studien:

Studienergebnisse:

Diagnostic performance of studies with ECA-MRI and EOB-MRI

For the ECA-MRI in 12 studies (13 outcomes), with 509 patients including 656 focal hepatic lesions, eight studies considered arterial hyperenhancement and subsequent washout appearance as indicative findings of viable tumors; three studies employed LI-RADS treatment response algorithm and one study used arterial hyperenhancement as diagnostic criteria. The sensitivity and specificity ranged 68–100% and 70–100%,

respectively. The pooled sensitivity and specificity for the diagnosis of post-treated HCC were 87% (95% CI 80–91) and 92% (95% CI 86–95), respectively (Fig. 2), with an area under the HSROC of 0.95 (95% CI 93–97; Fig. 3a). For the EOB-MRI in 5 studies (6 outcomes), with 294 patients including 362 focal hepatic lesions, two studies utilized arterial hyperintensity, and hypointensity on PVP and/or DP and/or HBP as diagnostic criteria; two studies regarded hypointensity on PVP and/or DP and/or HBP and one study employed hypointensity on HBP as diagnostic criteria. The sensitivity and specificity ranged 25–97% and 73–100%, respectively. The pooled sensitivity and specificity for the diagnosis of HCC were 79% (95% CI 64–89) and 96% (95% CI 78–99), respectively (Fig. 4), with an area under the HSROC of 0.92 (95% CI 89–94; Fig. 3b). Furthermore, compared with ECA-MRI, no significant difference was found in the pooled sensitivity (87% [ECA-MRI] vs. 79% [EOB-MRI]) or specificity (92% vs. 96%, P = 0.41; Table 2).

There was substantial study heterogeneity noted in the sensitivity (I2 = 49% and 72%, respectively) and specificity (I2 = 42% and 74%, respectively) in both ECA-MRI studies and EOB-MRI studies (All P < 0.1).

Comparison of diagnostic performance in the subgroups

The results of the subgroup analyses are summarized in Table 2. Regarding study design, ECA-MRI had higher sensitivity and specificity than EOB-MRI in prospective studies (93% vs. 71% [sensitivity], 98% vs. 95%[specificity]), but higher sensitivity and lower specificity than EOB-MRI in retrospective studies (86% vs. 80% [sensitivity], 89% vs. 94% [specificity]. However, no significant difference was found between them (both P > 0.05). Regarding type of LRT, the sensitivity of ECA-MRI was lower than EOB-MRI (88% vs. 89%) in the subgroup of 'TACE', while higher than EOB-MRI (72% vs. 71%) in the subgroup of 'Ablation'. The specificity of ECA-MRI was lower than EOB-MRI in both subgroups (93% vs. 96%, 85% vs. 97%), and we found no difference between them (both P > 0.05). Regarding the most common etiology of liver disease, there was no significant difference between ECA-MRI and EOB-MRI in both 'Hepatitis C' and 'Hepatitis B' groups (77% vs. 71% [sensitivity], and 90% vs. 95%[specificity] in hepatitis C, P = 0.69; 91% vs. 83% [sensitivity], and 84% vs. 98%[specificity] in hepatitis B, P = 0.50). Similarly, no significant difference was found between ECA-MRI and EOB-MRI in the subgroups of 'Baseline lesion size' (88% vs. 76% [sensitivity], and 87% vs. 95%[specificity] in lesion size ≤ 3 cm, P = 0.98; 89% vs. 97% [sensitivity], and 97% vs. 100%[specificity] in lesion size > 3 cm, P = 0.26), 'Time of post-treated examination' (89% vs. 79% [sensitivity], and 93% vs. 93%[specificity] in time ≤ 1 month, P = 0.73; 91% vs. 93% [sensitivity], and 96% vs. 100%[specificity] in time > 1 month, P = 0.34) and 'MRI field strength' (93% vs. 82% [sensitivity], and 96% vs. 99%[specificity] in 3.0 T only, P = 0.76; 81% vs. 64% [sensitivity], and 89% vs. 82%[specificity] in 1.5 T or combined use, P = 0.32).

Meta regression analysis

Meta regression was performed to explore the potential sources of heterogeneity. In the meta-regression analysis, the five factors of Study design, type of LRT, most common etiology of liver disease, baseline lesion size, and time of post-treated examination (All Ph < 0.05) were significantly associated with heterogeneity across the studies using ECA-MRI. the two factors of most common etiology of liver disease and MRI field strength (both Ph = 0.02) were significantly associated with heterogeneity across the studies using EOB-MRI.
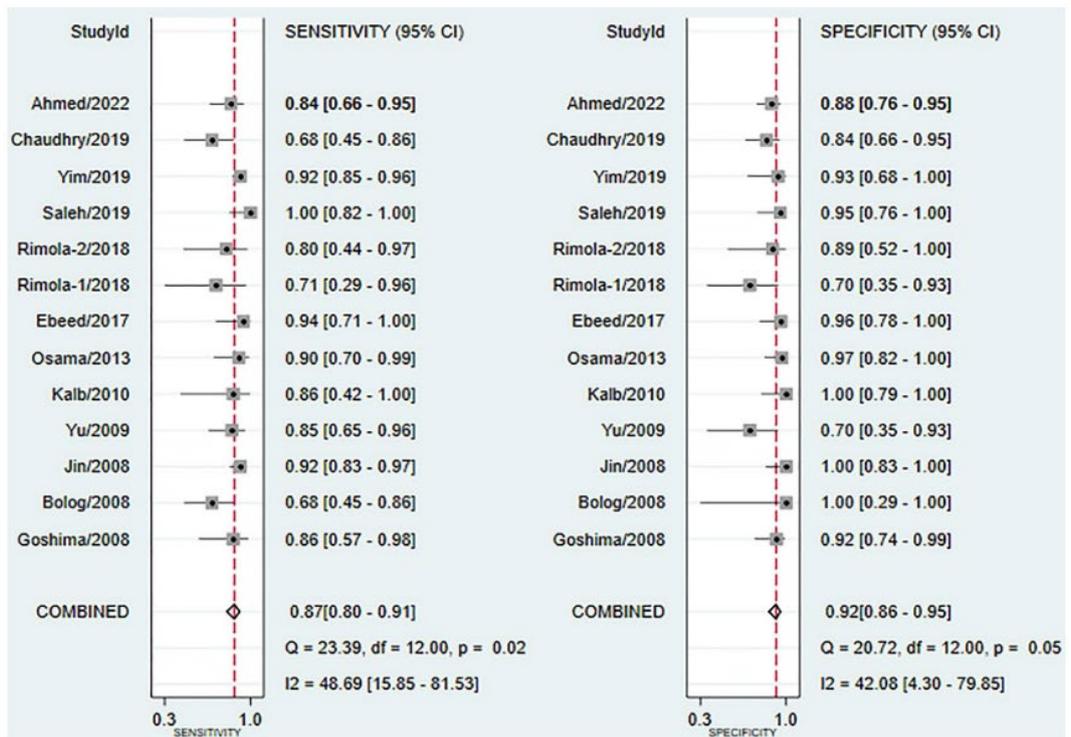
Fig. 2 Forest plots of sensitivity and specificity for the diagnosis of post-treated HCC using extracellular contrast agent (ECA)
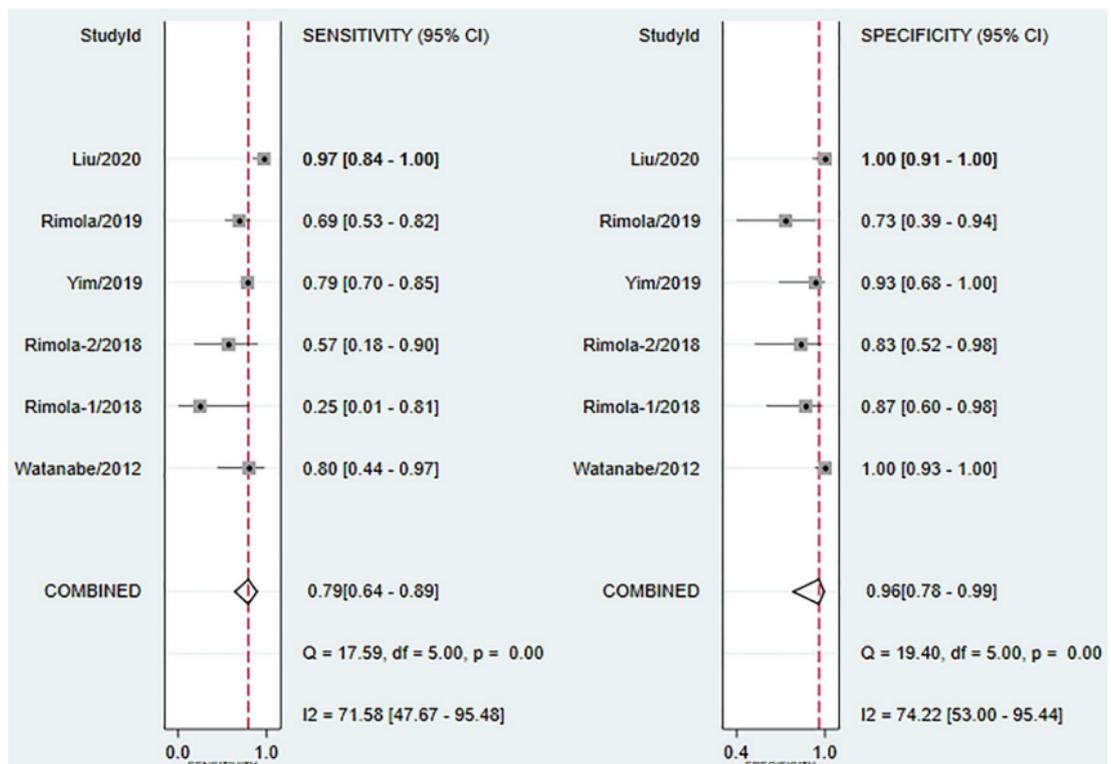

Fig. 4 Forest plots of sensitivity and specificity for the diagnosis of post-treated HCC using hepatobiliary contrast agent (EOB)

Table 2 Comparison of pooled diagnostic performance between ECA—MRI and EOB – MRI after LRT

	No. of studies (n = ECA-MRI, EOB-MRI)	No. of lesions (n = ECA-MRI, EOB-MRI)	Sensitivity (%) (95% CI)		Specificity (%) (95% CI)		P
			ECA–MRI	EOB–MRI	ECA–MRI	EOB–MRI	
Total	13, 6	656, 362	87 (80–91)	79 (64–89)	92 (86–95)	96 (78–99)	0.41
Study design							
Prospective	3, 2	155, 114	93 (86–97)	71 (60–83)	98 (91–100)	95 (87–99)	0.23
Retrospective	10, 4	501, 248	86 (81–89)	80 (73–86)	89 (84–93)	94 (87–98)	0.74
Type of LRT							
TACE	9, 2	369, 93	88 (83–92)	89 (75–97)	93 (88–97)	96 (88 – 100)	0.82
Ablation	2, 2	70, 80	72 (53–86)	71 (44–90)	85 (70–94)	97 (89–100)	0.34
Most common etiology of liver disease							
Hepatitis C	5, 2	226, 114	77 (67–85)	71 (60–83)	90 (83–94)	95 (87–99)	0.69
Hepatitis B	2, 2	172, 210	91 (85–95)	83 (76–88)	84 (64–96)	98 (90–100)	0.50
Baseline lesion size							
≤3 cm	2, 3	199, 341	88 (82–93)	76 (69–82)	87 (74–95)	95 (87–99)	0.98
> 3 cm	6, 1	203, 266	89 (83–94)	97 (84–100)	97 (92–99)	100 (91–100)	0.26
Time of post–treated examination							
≤1 month	6, 1	350, 136	89 (84–93)	79 (70–85)	93 (87–97)	93 (68–100)	0.73
>1 month	2, 2	131, 135	91 (83–96)	93 (81–98)	96 (85–99)	100 (96–100)	0.34
MRI field strength							
3.0 T only	3, 3	176, 271	93 (88–96)	82 (76–88)	96 (88–99)	99 (95–100)	0.76
1.5 T or combined use	10, 3	388, 91	81 (75–88)	64 (50–78)	89 (84–93)	82 (66–92)	0.32

CI confidence interval, *LRT* locoregional therapies, *ECA* extracellular contrast agent, *EOB* hepatobiliary contrast agent

Anmerkung/Fazit der Autoren

In conclusion, our meta-analysis demonstrated that ECAMRI yield overall comparable sensitivity and specificity to EOB-MRI for the diagnosis of residual or recurrent HCC after LRT. Furthermore, no significant difference in performance was found according to study design, type of LRT, most common etiology of liver disease, baseline lesion size, time of post-treated examination and MRI field strength. Prioritizing the accurate diagnosis and effective management of post-treated HCC is crucial. Given the similar diagnostic performance of ECA-MRI and EOBMRI, further prospective multi-center studies with direct comparisons are warranted to determine the ideal contrast agent tailored to individual patient characteristics.

Kommentare zum Review

Das SR erfüllt nicht ausreichend die methodischen Anforderungen. Aufgrund fehlender höherwertiger Evidenz wird es jedoch ergänzend dargestellt.

3.3 Leitlinien

Johnson DR et al., 2022 [2].

American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS)

Congress of Neurological Surgeons systematic review and evidence-based guidelines update on the role of imaging in the management of progressive glioblastoma in adults

Zielsetzung/Fragestellung

"The purpose of this guideline update is to assess the ability of imaging techniques to aid in the management of patients with previously treated glioblastoma, specifically by differentiating tumor recurrence from treatment-related change."

Methodik

Hier beschrieben: https://www.cns.org/guidelines/guideline-development-methodology

Grundlage der Leitlinie

- Repräsentatives Gremium: ja
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: (ja)
- Systematische Suche, Auswahl und Bewertung der Evidenz: ja
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: nein
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: ja
- Regelmäßige Überprüfung der Aktualität gesichert: update der LL von 2014

Recherche/Suchzeitraum:

- Recherche in Pubmed, Embase, Cochrane Library im März 2019, nur englischsprachige Artikel

LoE/GoR

Class I Evidence Level I (or A) Recommendation	Evidence provided by one or more well-designed clinical studies of a diverse population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
Class II Evidence Level II (or B) Recommendation	Evidence provided by one or more well-designed clinical studies of a restricted population using a "gold standard" reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
Class III Evidence Level III (or C) Recommendation	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.

- Class I:

- o Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference "gold" standard)
- o Systematic review of Class I studies
- Class II:
  - o Development of diagnostic criteria on consecutive patients (with universally applied reference "gold" standard)
  - o Systematic review2 of Class II studies
  - o Study of nonconsecutive patients; without consistently applied "gold" standard
  - o Systematic review2 of Class III studies
- Class III:
  - o Case-control study
  - o Poor reference standard
  - o Expert Opinion

Empfehlungen

Empfehlung 1 (Level II)

Magnetic resonance imaging with and without gadolinium enhancement is recommended as the imaging surveillance method to detect the progression of previously diagnosed glioblastoma.

Empfehlung 2 (Level III)

Magnetic resonance perfusion is suggested as a diagnostic method to differentiate true tumor progression from treatment-related imaging changes or pseudo-progression in patients with suspected progressive glioblastoma.

Hinweis

Keine spezifischen Empfehlungen für Kontrastmittel

Ian Paterson et al., 2021 [1].

Canadian Cardiovascular Society; Canadian Society for Cardiovascular Magnetic Resonance; Canadian Heart Rhythm Society

2021 Update on Safety of Magnetic Resonance Imaging: Joint Statement From Canadian Cardiovascular Society/Canadian Society for Cardiovascular Magnetic Resonance/Canadian Heart Rhythm Society

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium – **trifft teilweise zu**;
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt – **trifft teilweise zu**;
- Systematische Suche, Auswahl und Bewertung der Evidenz – **trifft teilweise zu**;
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt – **trifft teilweise zu**;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt – **trifft zu**;

- Regelmäßige Überprüfung der Aktualität gesichert – **unklar**.

<u>Recherche/Suchzeitraum:</u>

- Additionally, an independent and relevant literature review and appraisal of the evidence was performed by the Canadian Agency for Drugs and Technologies in Health
- Medline, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search
- published between Jan 1, 2010 and March 5, 2019.

<u>LoE/GoR</u>

- GRADE

Empfehlungen

Use of Gadolinium-Based Contrast Agents

NSF is an often progressive disease that has been reported in patients with renal insufficiency and previous gadolinium exposure. It is typically characterized by thickening of the skin, especially of the arms and legs, and is associated with reduced range of motion. Rarely, NSF might also involve skeletal muscles, the diaphragm, dura, or mesothelium. To reduce the potential for this rare toxicity GBCAs are routinely bound to ligands using either a linear or macrocyclic molecular structure. According to the definition provided in the Canadian Association of Radiologists guidelines, or the American College of Radiology's classification of GBCAs, group I agents refer to older linear agents most commonly associated with NSF, group II agents refers to newer linear agents and some macrocyclic agents with few if any associated cases of NSF, and group III agents refer to macrocyclic agents with limited data on possible association with NSF (Table 1). Estimation of risk is on the basis of the presence of renal dysfunction, defined by the eGFR, which is calculated from serum creatinine using either the Chronic Kidney Disease Epidemiology Collaboration equation or the Modification of Diet in Renal Disease study equation. The following recommendations pertain to use of GBCAs in adults, defined as 18 years of age or older.

Table 1. The American College of Radiology manual classification of gadolinium-based agents and recommended use in patients with renal dysfunction

Group	Gadolinium-based contrast agent	Use of GBCA
Group I ("older linear agents"); agents associated with the greatest number of NSF cases	Gadodiamide (Omniscan; GE Healthcare, Chicago, IL) Gadopentetate dimeglumine (Magnevist; Bayer HealthCare Pharmaceuticals, Whippany, NJ) Gadoversetamide (OptiMARK, Guerbet, Villepinte, France)	Contraindicated in patients with eGFR < 30 mL/min/1.73 m^2
Group II ("newer linear and macrocyclic agents"); agents associated with few, if any, unconfounded cases of NSF	Gadobenate dimeglumine (MultiHance; Bracco Diagnostics, Monroe Township, NJ) Gadobutrol (Gadavist; Bayer HealthCare Pharmaceuticals; Gadovist in many countries) Gadoterate acid (Dotarem; Guerbet) Gadoteridol (ProHance; Bracco Diagnostics)	Can be safely administered for patients with eGFR between 30 and 90 mL/min/1.73 m^2 Consider on case-by-case basis for patients with acutely unstable renal function (AKI), eGFR < 30 mL/min/1.73 m^2 and/or receiving dialysis
Group III ("macrocyclic agents"); agents for which data remain limited regarding NSF risk, but for which few, if any unconfounded cases of NSF have been reported	Gadoxetate disodium (Eovist; Bayer HealthCare Pharmaceuticals; Primovist in many countries)	

AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; GBCA, gadolinium-based contrast agent; NSF, nephrogenic systemic fibrosis. Table derived from McDonald et al.[35] American College of Radiology,[36] and Schieda et al.[37]

> **RECOMMENDATION**
>
> 12. We recommend that when GBCAs are used, macrocy-clic or newer linear agents (group II or III) are used in preference to older linear agents (group I) (Strong Recommendation; High-Quality Evidence).
>
> **Values and preferences.** Nearly all nonadjudicated cases of NSF have been reported after exposure to first-generation group I linear agents, whereas few, if any, have been associated with group II or III agents.[38-40]

As a class, macrocyclic GBCAs have greater kinetic stability than linear agents, leading to lower amounts of gadolinium tissue retention.[41] Nonallergic toxicity results from direct cellular effects of gadolinium salts and competition with calcium-dependent biologic processes; gadolinium chelates (including GBCAs) do not have the same effect.[35] However, macrocyclic agents appear to be associated with a higher rate of allergic-like adverse events in patients injected with GBCAs.[42]

Group I agents are contraindicated in patients with an eGFR < 30 mL/min/1.73 m2.[43,44] The risk of NSF with these agents in patients with acute kidney injury (AKI) or severe renal impairment is estimated between 1% and 7%.[36] However, at the present time, there is insufficient evidence to recommend macrocyclic agents (gadoteridol, gadobutrol, gadoteric acid) over newer linear agents (gadobenate dimeglumine, gadoxetate disodium) to reduce the risk of NSF or gadolinium tissue retention.[45]

Practical tip. We suggest that the lowest dose of GBCA required to obtain the needed clinical information should be used only when necessary, and that institutions internally review which GBCAs are used locally to establish a safe time interval before repeated administration. Regular vendor-suggested dosing is recommended according to body surface area and the indication for the study.[46-48] Half- or quarter-dosing is not recommended because of the possibility of obtaining nondiagnostic images and double-dosing should be avoided unless for LGE imaging or large vessel angiography, where it is routinely used. Patients should not receive multiple doses of GBCA until sufficient time has passed to allow for excretion, as determined by individual institutions and clinical necessity. In general, at least 24 hours is suggested between repeat dosing in those with normal renal function; > 90% of each delivered dose is excreted in the urine by 12 hours[46] or 24 hours[47,48] and longer in those with impaired renal function. When repeat studies are anticipated, the use of group II or III agents are recommended.

Overall, for patients with an eGFR between 30 and 90 mL/min/1.73 m2, group II or III GBCAs can be safely administered. For patients with mild renal impairment (eGFR between 60 and 90 mL/min/1.73 m2), there is no evidence to suggest an increased risk of NSF and no special precautions, including screening, are required before group II or III GBCA administration.[48] The risk of developing NSF with moderate renal impairment (eGFR between 30 and 60 mL/min/1.73 m2) is exceedingly low, and in these patients, group II and III GBCAs can also be administered safely without any substantial risk of developing NSF, need for screening or informed consent, recognizing that consent might still be considered for other reasons.[37] Although the association between NSF development and exposure to GBCAs is most likely to occur in those with impaired renal function, in reports of NSF in patients with moderate renal dysfunction, it generally occurred in those with AKI.[49,50] Screening in this population with either questionnaires or eGFR is resource-consuming, and a potential barrier to timely and appropriate investigation. Patients taking part in research studies should adhere to these criteria and principles.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 01 of 12, January 2026) am 05.01.2026

#	Suchschritt
1	[mh "Magnetic Resonance Imaging"]
2	((MR AND (imag* OR scan* OR tomogr*)) OR MRI OR MRT OR "magnetic resonance" OR NMR OR NMRI OR NMRT OR FMRI OR FMRT OR MRA OR (chemical NEXT shift NEXT imag*) OR "proton spin" OR "spin echo"):ti,ab,kw OR MR:ti
3	#1 OR #2
4	[mh "Contrast media"]
5	(Contrast* OR Radiocontrast OR Radiopaque):ti,ab,kw OR enhanced:ti
6	#4 OR #5
7	#3 AND #6
8	#7 with Cochrane Library publication date from Jan 2021 to present, in Cochrane Reviews
9	#7 with Cochrane Library publication date from Jan 2024 to present, in Cochrane Reviews
10	#8 NOT #9

Leitlinien und systematische Reviews in PubMed am 05.01.2026

verwendete Suchfilter für Leitlinien:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 21.06.2017.

verwendeter Suchfilter für systematische Reviews:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 01.01.2026.

#	Suchschritt
	Leitlinien
1	Magnetic Resonance Imaging [mh]
2	(MR[tiab] AND (imag*[tiab] OR scan*[tiab] OR tomogr*[tiab])) OR MRI[tiab] OR MRT[tiab] OR magnetic resonance[tiab] OR NMR[tiab] OR NMRI[tiab] OR NMRT[tiab] OR FMRI[tiab] OR FMRT[tiab] OR MRA[tiab] OR chemical shift imag*[tiab] OR proton spin[tiab] OR spin echo[tiab] OR MR[ti]
3	#1 OR #2
4	Contrast Media[pa]
5	Contrast*[tiab] OR Radiocontrast[tiab] OR Radiopaque[tiab] OR enhanced[ti]
6	#4 OR #5
7	#3 AND #6

#	Suchschritt
8	(#7) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[ti] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
9	(#8) AND ("2021/01/01"[PDAT] : "3000"[PDAT])
10	(#9) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews
11	(#7) AND ("systematic review"[pt] OR "meta-analysis"[pt] OR "network meta-analysis"[pt] OR (systematic*[tiab] AND (review*[tiab] OR overview*[tiab])) OR metareview*[tiab] OR umbrella review*[tiab] OR "overview of reviews"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR metanaly*[tiab] OR meta-synthes*[tiab] OR metasynthes*[tiab] OR meta-study[tiab] OR metastudy[tiab] OR integrative review[tiab] OR integrative literature review[tiab] OR evidence review[tiab] OR (("evidence-based medicine"[mh] OR evidence synthes*[tiab]) AND "review"[pt]) OR ((("evidence based"[tiab:~3]) OR evidence base[tiab]) AND (review*[tiab] OR overview*[tiab])) OR (review[ti] AND (comprehensive[ti] OR studies[ti] OR trials[ti])) OR ((critical appraisal*[tiab] OR critically appraise*[tiab] OR study selection[tiab] OR ((predetermined[tiab] OR inclusion[tiab] OR selection[tiab] OR eligibility[tiab]) AND criteri*[tiab]) OR exclusion criteri*[tiab] OR screening criteri*[tiab] OR systematic*[tiab] OR data extraction*[tiab] OR data synthes*[tiab] OR prisma*[tiab] OR moose[tiab] OR entreq[tiab] OR mecir[tiab] OR stard[tiab] OR strobe[tiab] OR "risk of bias"[tiab]) AND (survey*[tiab] OR overview*[tiab] OR review*[tiab] OR search*[tiab] OR analysis[ti] OR apprais*[tiab] OR research*[tiab] OR synthes*[tiab]) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR bibliographies[tiab] OR published[tiab] OR citations[tiab] OR database*[tiab] OR references[tiab] OR reference-list*[tiab] OR papers[tiab] OR trials[tiab] OR studies[tiab] OR medline[tiab] OR embase[tiab] OR cochrane[tiab] OR pubmed[tiab] OR "web of science" [tiab] OR cinahl[tiab] OR cinhal[tiab] OR scisearch[tiab] OR ovid[tiab] OR ebsco[tiab] OR scopus[tiab] OR epistemonikos[tiab] OR prospero[tiab] OR proquest[tiab] OR lilacs[tiab] OR biosis[tiab])) OR "technical report"[pt] OR HTA[tiab] OR technology assessment*[tiab] OR technology report*[tiab])
12	(#11) AND ("2021/01/01"[PDAT] : "3000"[PDAT])
13	(#12) NOT "The Cochrane database of systematic reviews"[Journal]
14	(#13) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews ohne Leitlinien
15	(#14) NOT (#10)
16	(#15) AND ("2024/01/01"[PDAT] : "3000"[PDAT])
17	#15 NOT #16

Iterative Handsuche nach grauer Literatur, abgeschlossen am 07.01.2026

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)

- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)

- ECRI Guidelines Trust (ECRI)
- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

Referenzen

1. **Ian Paterson D, White JA, Butler CR, Connelly KA, Guerra PG, Hill MD, et al.** 2021 update on safety of magnetic resonance imaging: joint statement from Canadian Cardiovascular Society/Canadian Society for Cardiovascular Magnetic Resonance/Canadian Heart Rhythm Society. Can J Cardiol 2021;37(6):835-847.

2. **Johnson DR, Glenn CA, Javan R, Olson JJ.** Congress of Neurological Surgeons systematic review and evidence-based guidelines update on the role of imaging in the management of progressive glioblastoma in adults. J Neurooncol 2022;158(2):139-165.

3. **Zhou S, Wang S, Xiang J, Han Z, Wang W, Zhang S, et al.** Diagnostic performance of MRI for residual or recurrent hepatocellular carcinoma after locoregional treatment according to contrast agent type: a systematic review and meta-analysis. Abdom Radiol (NY) 2024;49(2):471-483.

[A] **Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al.** PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev 2021;10(1):39. https://doi.org/10.1186/s13643-020-01542-z

[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

- keine eingegangenen schriftlichen Rückmeldungen gem. § 7 Absatz 6 VerfO