

Original Article

Magnetic resonance-guided ablation of liver tumors: A systematic review and pooled analysis

ABSTRACT

Purpose: The purpose of this study is to study the clinical outcomes of different types of magnetic resonance (MR)-guided ablation for the treatment of liver tumors by performing a systematic review and pooled analysis.

Materials and Methods: A comprehensive literature search was performed for clinical trials published from January 1997 to October 2019 in PubMed, the Web of Science, Embase, and the Cochrane Library. Pooled analyses were performed to obtain the complete ablation (CA), complication, progression-free survival (PFS), and overall survival (OS) rates.

Results: Thirty studies were eligible, including four studies on MR-guided microwave ablation (MWA); 14 studies on MR-guided radiofrequency ablation (RFA); one study on both MR-guided MWA and RFA; eight studies on MR-guided, laser-induced thermotherapy (LITT); two studies on MR-guided percutaneous cryoablation (PC); and one study on MR-guided percutaneous ethanol injection (PEI). The CA rates in patients who underwent RFA, MWA, LITT, PC, and PEI were 95.60%, 98.86%, 77.78%, 47.92%, and 85.71%, respectively. The most frequent complications were pain (27.66%, 13/47) and postablation syndrome (27.66%, 13/47) in the PC group; pleural effusion (8.11%, 119/1,468) and subcapsular hematoma (2.25%, 33/1,468) in the LITT group; pleural effusion (2.67%, 2/75) in the MWA group; and subcapsular hematoma (4.18%, 20/478) and post-ablation syndrome (2.93%, 14/478) in the RFA group. There were few studies reporting PFS and OS.

Conclusions: MR-guided ablation is a practicable alternative treatment for liver tumors, especially MR-guided RFA and MWA, which have high rates of CA and low occurrences of complications.


KEY WORDS: Ablation, liver tumors, magnetic resonance guidance, pooled analysis, systematic review

INTRODUCTION

Currently, hepatocellular carcinoma (HCC) is the sixth most common cancer in the world and is the third leading cause of cancer-related deaths.^[1] The incidence and mortality rates of HCC are projected to further increase in coming decades. In addition, approximately 40%–70% of patients with colorectal cancer and 4%–14% of patients with gastric cancer develop hepatic metastases during the course of their diseases, and their prognosis is relatively poor.^[2,3] However, only a minority of patients with

either primary or secondary liver tumors are the candidates for resection because they have impaired liver function or concurrent disease.^[4] Image-guided ablation methods, including percutaneous ethanol injection (PEI), laser-induced thermotherapy (LITT), radiofrequency ablation (RFA), and microwave ablation (MWA), have been used in the treatment of nonsurgical patients with primary or metastatic liver tumors.^[5-9]

Magnetic resonance imaging (MRI) is widely accepted in interventional therapy due to its sensitivity to temperature and ability to provide multi-parametric images and its better image

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quality over other techniques. It provides good soft-tissue contrast and is usable even when a bone or an air space lies between the probe and the target. In addition, MRI can noninvasively monitor tissue temperature changes and provide three-dimensional orientation during surgery. As noted above, MRI has been increasingly used for several different methods of guiding ablation. However, owing to the lack of such studies, we performed a systematic review and pooled analysis to evaluate the safety and efficacy of the different magnetic resonance (MR)-guided ablation methods used in the treatment of liver tumors.

MATERIALS AND METHODS

Using the PubMed, Web of Science, Embase, and Cochrane Library databases, a comprehensive literature search was performed for clinical trials published from January 1997 to October 2019. Specific search terms included the following: (liver tumor OR liver cancer OR liver neoplasm OR HCC), (MRI OR MR imaging OR MR-guided OR MRI) and ablation. Reference lists from retrieved articles were searched for additional studies that may have been missed during the database searches.

Inclusion and exclusion criteria

To be eligible for analysis, studies had to include the following: (1) patients with primary or metastatic liver tumors; (2) MR-guided ablation treatment; and (3) information on the outcomes of patients who underwent these treatments. Outcome data included complication rates, complete ablation (CA) rates, and prognostic information. Case reports, review articles, articles using animal models, articles not about MR-guided ablation, unpublished data, and publications in languages other than English were excluded from the analysis.

Data extraction

Two investigators (Jianfeng Xiang and Ming Liu) reviewed and identified articles for review. The extracted data, including study characteristics, study population, technical details, and outcome measurements, were recorded using a standardized excel file, and a consensus regarding eligibility was reached on all items.

Data analysis

For the rates of complications, CA, progression-free survival (PFS) and overall survival (OS), proportions and 95% confidence intervals (CIs) were calculated using a binomial distribution. A pooled analysis was used to determine the weighted summary statistics for each of the treatments. Results were

presented as pooled proportions for the complication, CA, and survival rates, with 95% CIs. All analyses were done with the R language (www.r-project.org).

RESULTS

Literature search

A flow diagram of our literature search is shown in Figure 1. A keyword-based search of the PubMed, Web of Science, Embase, and Cochrane Library databases identified a total of 1615 citations, 421 of which were excluded for being duplicates. After title and abstract review, 1045 studies were excluded for various reasons (759 were not about MR-guided ablation, 141 were reviews, 60 were single case reports, and 85 were about animal models). The full text of the remaining 149 articles and an additional seven studies extracted from references was retrieved for more detailed assessment. One hundred and twenty-six of these studies did not have data about the outcomes of treatment or did not involve MR-guided

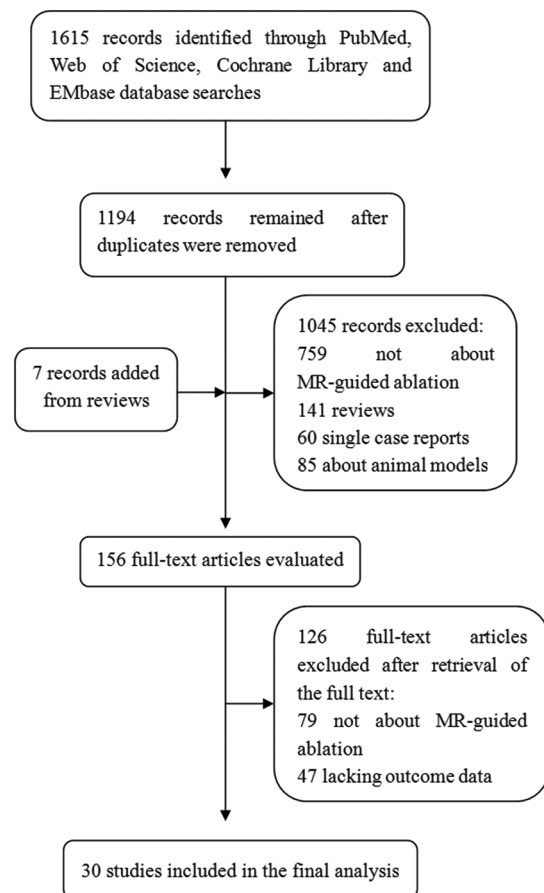


Figure 1: A flow chart showing the selection of studies for the analysis

ablation and were subsequently excluded. As a result, 30 studies were included in the final meta-analysis.

Study characteristics

Baseline characteristics of the included studies are summarized in Table 1. The 30 studies were published between January 1997 and October 2019 and involved a total of 2,075 patients. Five studies reported a total of 75 patients treated with MR-guided MWA, 15 described 478 treated with MR-guided RFA, eight provided data for 1,468 treated with MR-guided LITT, two reported findings for a total of 47 treated with MR-guided percutaneous cryoablation (PC), and one described seven treated with MR-guided PEI. Of these 30 studies, 17 were conducted in Germany, five in Japan, two in China, two in Switzerland, one in the USA, one in South Korea, one in Austria, and one in England. Details of the studies are shown in Table 1.

Complete ablation rates

Twenty-two studies reported the CA rate after treatment, including one of PEI,^[39] two of PC,^[37,38] two of LITT,^[30,35] four of MWA,^[10,11,13,14] and 14 of RFA.^[10,15-27] The pooled data showed that the CA rates in patients who underwent RFA, MWA, PEI, LITT, and PC were 95.60%, 98.86%, 85.71%, 77.78%, and 47.92%, respectively [Figure 2].

Occurrence of complications

Table 2 lists the main adverse events that occurred among the different MR-guided ablation treatments. The main complications reported were pain (27.66%, 13/47) and postablation syndrome (27.66%, 13/47) in the PC group; pleural effusion (8.11%, 119/1,468) and subcapsular hematoma (2.25%, 33/1468) in the LITT group; pleural effusion (2.67%, 2/75) in

the MWA group; and subcapsular hematoma (4.18%, 20/478) and postablation syndrome (2.93%, 14/478) in the RFA group.

Progression-free survival rates

Only nine studies evaluated PFS rates, including two analyses about LITT, both of which reported the 3- and 6-month PFS rates,^[33,34] and one of which included the 12-month PFS rate.^[33] There were seven other studies that reported the 12-month PFS rates, including one about PEI,^[39] two about MWA,^[12,14] and four about RFA.^[15,17,18,21]

As shown in Figure 3, when we pooled the two LITT studies, we found that their 3- and 6-month PFS rates and 95% CIs were 98.72% (97.95%–99.49%) and 96.98% (95.96%–98.00%), respectively. The 12-month PFS rate and 95% CI were 85.71% (60.20%–100%) in the PEI study, 63.79% (56.00%–71.60%) in the pooled RFA studies, 69.40% (57.60%–81.20%) in the LITT study, and 47.22% (31.50%–62.90%) in the pooled MWA studies.

Overall survival rate

Six studies reported the OS rates.^[12,15,17,29,37,38] Five studies (147 patients) reported the 1-year OS, five (121 patients) the

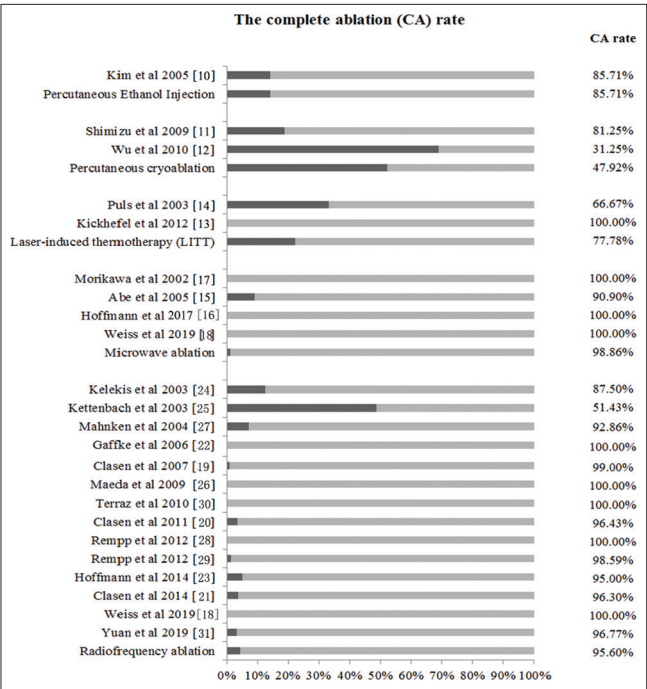


Figure 2: The complete ablation rates among the included studies

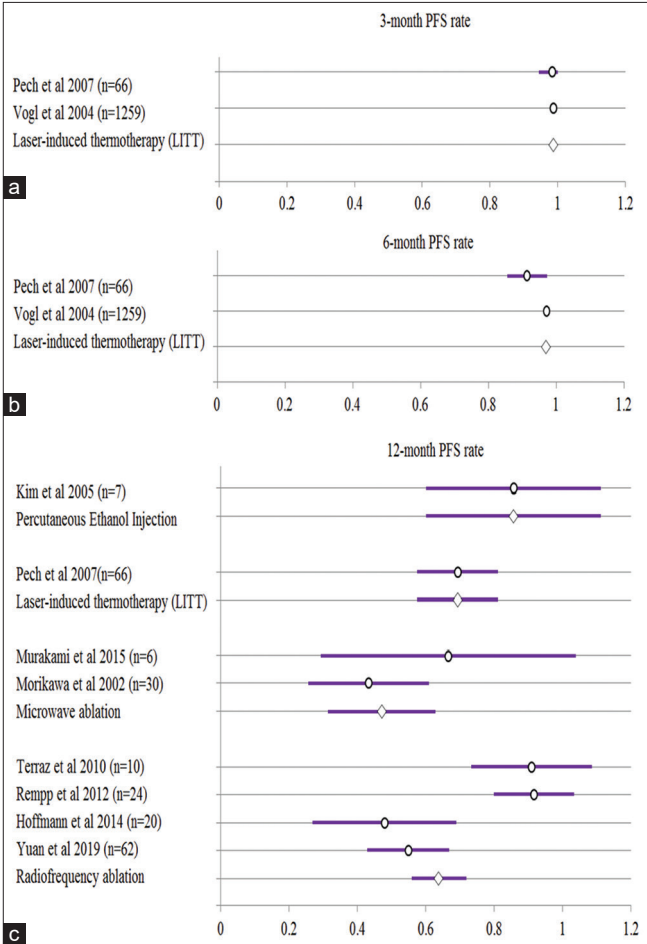


Figure 3: The PFS rates and 95% confidence intervals for the studies. The PFS rates are shown for (a) 3 months, (b) 6 months, and (c) 12 months. PFS = Progression-free survival

Table 1: Characteristics of each study included in the analysis

Author	Year	Country	Patients (n)	Age (mean, years)	Liver cirrhosis (B:C)	Child-pugh (A:B)	Tumors (n) (HCC/ Met)	Tumor size (cm)	Treatment	Field strength	Follow-up (months)
Weiss <i>et al.</i> ^[10]	2019	Germany	45 (RFA 27; MWA 16)	61.1	NA	NA	47 (11.36)	0.9±0.21	RFA	1.5 T	24.7±14.0
Hoffmann <i>et al.</i> ^[11]	2017	Germany	15	59.8	NA	NA	18 (7.11)	1.54±0.77	MWA	1.5 T	5.8±2.6
Murakami <i>et al.</i> ^[12]	2015	Japan	6	65.3	6 (3:3)	3:3	9	2.08±0.54	Laparoscopic microwave coagulation therapy	0.5 T	NA
Abe <i>et al.</i> ^[13]	2005	Japan	8	49.0	NA	NA	11 (0.11)	NA	Microwave thermocoagulation therapy	0.5 T	25.9
Morikawa <i>et al.</i> ^[14]	2002	Japan	30	59.7 (Met)/63.1 (HCC)	NA	NA	30 (8.22)	NA	Microwave thermocoagulation therapy	0.5 T	16.9
Yuan <i>et al.</i> ^[15]	2019	China	62	57.43	53 (50:3)	61:1	63 (63.0)	2	RFA	0.35 T	>36
Clasen <i>et al.</i> ^[16]	2014	Germany	53	64.9	NA	NA	56 (56.0)	NA	RFA	1.5 T	22.9
Hoffmann <i>et al.</i> ^[17]	2014	Germany	20	69.6	2:5	18:2	NA	3.9±0.7	RFA	1.5 T	39.1±22.4
Rempp <i>et al.</i> ^[18]	2012	Germany	24	66	NA	NA	NA	NA	RFA	1.5 T	11.5±2.7
Rempp <i>et al.</i> ^[19]	2012	Germany	110	64	NA	NA	213	2	RFA	1.5 T	24.2
Clasen <i>et al.</i> ^[20]	2011	Germany	20	63.8	NA	17:3	28 (28.0)	2.8	RFA	0.2 T	24.2
Terraz <i>et al.</i> ^[21]	2010	Switzerland	10	63	NA	NA	NA	NA	RFA	1.5 T	NA
Maeda <i>et al.</i> ^[22]	2009	Japan	34	70.3	3:26	29:5	51	2.1±0.7	RFA	0.4 T	1-28
Clasen <i>et al.</i> ^[23]	2007	Germany	64	63.7	NA	NA	100 (19.81)	2.47±1.10	RFA	0.2 T	NA
Gaffke <i>et al.</i> ^[24]	2006	Germany	8	62.5	NA	NA	12 (0.12)	2.4±0.6	RFA	1.5 T	7
Mahnken <i>et al.</i> ^[25]	2004	Germany	10	63.7	NA	NA	14 (1.13)	3.3	RFA	1.5 T	12.2
Kettenbach <i>et al.</i> ^[26]	2003	Austria	26	58	NA	NA	48 (15.33)	2.9	RFA	0.2 T	1-2
Kelekis <i>et al.</i> ^[27]	2003	Switzerland	4	NA	NA	NA	8 (3.5)	2.0	RFA	0.23 T	4.4
Lewin <i>et al.</i> ^[28]	1998	USA	6	NA	NA	NA	6 (0.6)	NA	RFA	0.2 T	NA
Eichler <i>et al.</i> ^[29]	2014	Germany	18	57	NA	NA	NA	NA	LITT	NA	NA
Kickhefel <i>et al.</i> ^[30]	2012	Germany	6	64	NA	NA	6	3.95±1.34	LITT	NA	NA
Vogl <i>et al.</i> ^[31]	2008	Germany	40	62.5	NA	NA	NA	NA	LITT	1.5 T	NA
Zangos <i>et al.</i> ^[32]	2007	Germany	32	NA	NA	NA	NA	NA	LITT	NA	NA
Pech <i>et al.</i> ^[33]	2007	Germany	66	65	NA	NA	117 (0.117)	NA	LITT	NA	NA
Vogl <i>et al.</i> ^[34]	2004	Germany	1259	NA	NA	NA	3440	NA	LITT	NA	NA
Puls <i>et al.</i> ^[35]	2003	Germany	12	61	NA	NA	NA	NA	LITT	1.5 T	NA
Dick <i>et al.</i> ^[36]	2003	England	35	59.1	NA	NA	125	NA	LTA	NA	5.8
Wu <i>et al.</i> ^[37]	2010	China	32	58.7	NA	23:9	36 (36.0)	4.7±1.8	PC	0.35 T	5-12
Shimizu <i>et al.</i> ^[38]	2009	Japan	15	61.8	NA	14:1	16 (16.0)	2.5±0.8	PC	NA	36.6±12.1
Kim <i>et al.</i> ^[39]	2005	South Korea	7	67	NA	NA	7 (7.0)	2.1	Percutaneous ethanol injection	0.2 T	41

PC=Percutaneous cryoablation, LITT=Laser-induced thermotherapy, MWA=Microwave ablation, RFA=Radiofrequency ablation, NA=Not available, LTA=Laser thermal ablation, HCC=Hepatocellular carcinoma

Table 2: Complications associated with magnetic resonance-guided ablation

Complication	PC (n=47)	LITT (n=1468)	MWA (n=75)	RFA (n=478)
Total, n (%)	37 (78.72)	177 (12.06)	4 (5.33)	62 (12.97)
Pain	13	11	0	2
Pleural effusion	2	119	2	1
Subcapsular hematoma	0	33	0	20
Pneumothorax	1	0	1	1
Hemothorax	3	0	-	-
Thrombocytopenia	5	0	0	2
Intra-hepatic abscess	0	6	0	
Local infection (puncture site)	0	6	0	1
Hypotension	0	2	0	-
Bowel perforation	0	0	0	3
Bleeding	0	0	0	2
Biloma	0	0	0	4
Ascites	0	0	0	4
Intraperitoneal hemorrhage	0	0	0	5
Postablation syndrome	13	0	1	14
Postembolization syndrome	0	0	0	3

LITT=Laser-induced thermotherapy, MWA=Microwave ablation, RFA=Radiofrequency ablation, PC=Percutaneous cryoablation

3 year, and three (44 patients) the 5 year. The results are shown in Figure 4. The 1-, 3-, and 5-year OS estimates and their 95% CIs were 88.00% (72.30%–100%), 47.00% (23.50%–70.50%), and 17.00% (0%–34.60%) for LITT; 95.10% (91.20%–99.00%), 76.83% (67.00%–86.60%), and 27.00% (11.00%–51.00%) for RFA; not reported, 66.67% (29.40%–103.90%), and 33.33% (0%–70.60%) for MWA; and 91.49% (83.70%–99.30%), 79.3% (59.70%–98.90%), and not reported for PC.

DISCUSSION

Until recently, most patients with hepatic tumors were unable to undergo liver resection, and those who did had a poor prognosis because of advanced cancer or liver dysfunction. However, the development of novel, minimally invasive ablative treatments, including LITT, RFA, and MWA, has provided the better control of malignant hepatic disease.

Computed tomography (CT) and ultrasound (US), either separately or in combination, have typically been used as navigation tools for these ablation treatments.^[40,41] However, there are some disadvantages to these modalities. For example, CT guidance cannot be used for real-time monitoring and leads to considerable radiation exposure for the surgical team, especially when performed as an in-room procedure. US is also widely used as a real-time, image-guided modality; however, it is associated with image disturbances caused by the generation of micro-bubbles during ablation. Accordingly, real-time MR guidance has been used as a reliable and radiation-free monitoring tool for LITT, RFA, and MWA.^[14,15,25,28,31-33,36] Numerous studies have demonstrated the safety and efficacy of MR-guided ablation treatments.

No systematic and pooled analysis has been published about these approaches, to our knowledge, despite the apparent advantages of MR-guided ablation. To this end, the present study was conducted to summarize the safety, efficacy, and prognosis of these MR-guided ablation treatments. Of the

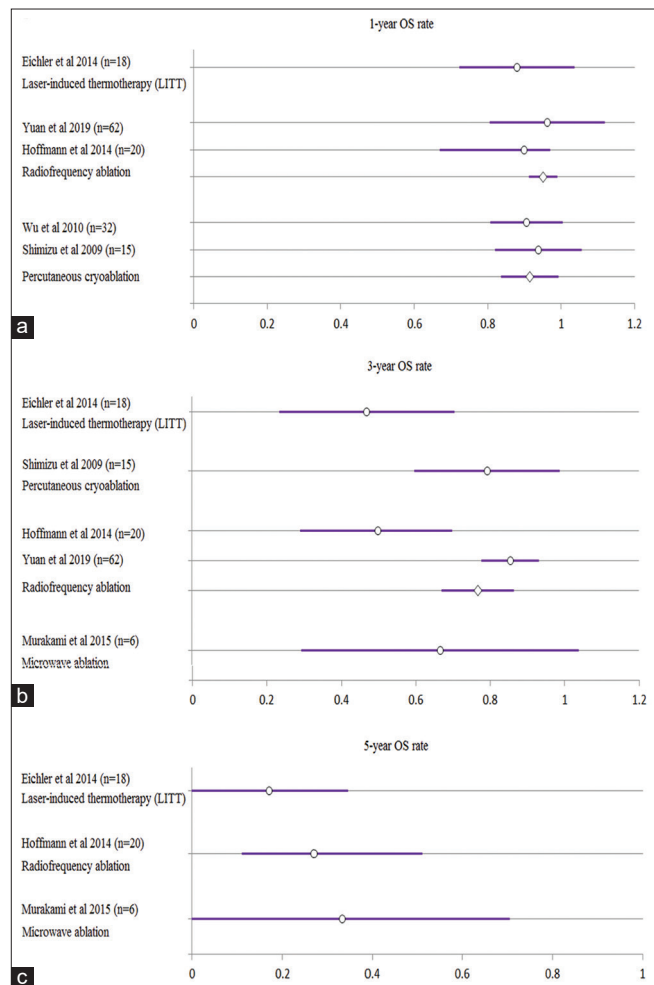


Figure 4: The OS rates and 95% confidence intervals for the studies. The OS rates at (a) 1 year, (b) 3 years, and (c) 5 years postprocedure OS = Overall survival

MR-guided ablation treatments, we found that MR-guided RFA studies were the most numerous with 15 related studies, while MR-guided LITT were the second most numerous with

eight. However, MR-guided MWA has been garnering more attention recently, with four out of five of the analyzed studies having been published after 2014. In addition, we found that MR-guided RFA and MWA have relatively high CA rates (>90%) and low occurrences of complications (<15%). However, few studies have reported the prognosis of PFS and OS. There are several limitations that need to be addressed. First, this was a systematic review and pooled analysis based on published studies – there is inherent heterogeneity among the different study populations, designs, and outcomes. Second, most MR-guided ablation studies reported a limited number of cases and without randomization or a control group. Third, the systems, sequences, and strengths of MR used in the different studies were different. This may be one reason for the different outcomes. Fourth, follow-up times were typically short, with the final overall prognosis missing from several studies. Although these limitations are significant, they are typical in the context of interventional studies performed with any new methods. In our view, this emphasizes the importance of pooled studies as a source of information regarding these techniques before their more widespread adaptation.

CONCLUSIONS

We systematically reviewed the outcomes of MR-guided ablation treatments and we suggest them for liver tumors as an alternative treatment, especially MR-guided RFA and MWA, which have high rates of CA and low occurrences of complications. However, studies with larger sample sizes and long-term prognosis are still needed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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