On-line Table 1: The characteristics of Gd-based contrast agents approved for MRI of the CNS

Trade Name, Generic Name (Acronym)	Dotarem, Gadoterate Meglumine (Gd-DOTA)	Gadavist, Gadobutrol (Gd-BT-DO3A)	Magnevist, Gadopentetate Dimeglumine (Gd-DTPA)	MultiHance, Gadobenate Dimeglumine (Gd-BOPTA)	ProHance, Gadoteridol (Gd-HP-DO3A)	Omniscan, Gadodiamide (Gd-DTPA-BMA)	OptiMARK, Gadoversetamide (Gd-DTPA-BMEA)
Company	Guerbet	Bayer	Bayer	Bracco	Bracco	GE Healthcare	Covidien
Doses (mmol/kg)[a]	0.1	0.1	0.1	0.1	0.1–0.3	0.1	0.1
Concentration (M)	0.5	1.0	0.5	0.5	0.5	0.5	0.5
Excess chelate (mg/mL)	0	0	0.4	0	0.2	12	331
Structure	Macrocyclic	Macrocyclic	Linear	Linear	Macrocyclic	Linear	Linear
Ionicity	Ionic	Nonionic	Ionic	Ionic	Nonionic	Nonionic	Nonionic
Osmolality (mOsm/kg H_2O, 37°C)	1350	1603	1960	1970	630	789	1110
Viscosity (mPas, 37°C)	2.0	5.0	2.9	5.3	1.3	1.4	2.0
Log K_{therm}	25.6	21.8	22.1	22.6	23.8	16.9	16.6
Log K_{cond}	19.3	14.7	17.7	18.4	17.1	14.9	15.0
Kinetic stability[b]	High	High	Low	Medium	High	Low	Low
Relaxivity (*r1*/*r2*, 1.5T) [c]							
Bovine plasma[d]	3.6/4.3	5.2/6.1	4.1/4.6	6.3/8.7	4.1/5.0	4.3/5.2	4.7/5.2
Human plasma[e]	N/A	4.7/7.5	3.9/5.3	7.9/18.9	N/A	N/A	N/A
Relaxivity (*r1*/*r2*, 3T)[c]							
Bovine plasma[d]	3.5/4.9	5.0/7.1	3.7/5.2	5.5/11.0	3.7/5.7	4.0/5.6	4.5/5.9
Human plasma[e]	N/A	4.5/6.3	3.9/5.2	5.9/17.5	N/A	N/A	N/A
Clearance	Renal	Renal	Renal	96% Renal, 4% hepatic	Renal	Renal	Renal

Note:—N/A indicates not applicable; K_{therm} = thermodynamic stability constant; K_{cond} = conditional stability constant.

[a] Approval for the highest dose indicated is dependent on country.

[b] Low: long-time index (defined in Laurent et al[15]) < 0.3; medium: long-time index 0.3–0.95; high: long-time index >0.95.

[c] Values in L $mmol^{-1}$ s^{-1} (plasma, 37°C).

[d] Taken from Rohrer et al.[11]

[e] Taken from Pintaske et al.[14]

On-line Table 2: Principal findings from prospective, intraindividual crossover studies of GBCAs at approved dose (0.1 mmol/kg body weight)

Reference	Comparison	No. Patients	Findings
Greco et al 2001[26]	Magnevist/ProHance @ 1/1.5T	80	No significant difference between Magnevist and ProHance for information provided on postcontrast images, including presence of disease, degree of enhancement, location and number of lesions, definition of lesion border, improved visualization, distinction of edema, disease classification, and detection of tumor recurrence; no significant difference in number of subjects for whom information prompted a change in diagnosis
Anzalone et al 2009[27]	Gadavist/Magnevist @ 1.5T	27	Improved lesion conspicuity after Gadavist in 10/27 cases vs 0/27 cases after Magnevist, and equivalent conspicuity in 17/27 cases ($P = .002$, Gadavist vs Magnevist)
Koenig et al 2013[30]	Gadavist/ProHance @ 1.5T	51	Greater subjective (qualitative) preference for Gadavist for contrast enhancement and diagnostic quality. Improved SNR on T1-FLASH images at 10 minutes postinjection but not on T1-SE or MPRAGE images
Anzalone et al 2013[32]	Gadavist/Dotarem @ 1/1.5T	136	Greater preference for Gadavist, both overall and for qualitative end points of lesion enhancement, but no difference for lesion delineation or for internal structure; greater lesion-to-brain contrast and percentage enhancement for Gadavist, but no difference in contrast-to-noise ratio between the 2 agents
FDA document[31]	Gadavist/ProHance @ 1/1.5T	380	Similar performances between Gadavist and ProHance in quality of visualization of CNS for both structures and lesions and for detection of lesions
Colosimo et al 2001[33]	MultiHance/Magnevist and Dotarem @ 1/1.5T	22	Sensitivity for lesion detection with MultiHance (93%–100%) markedly higher than comparator-enhanced examinations (65%–73%)
Knopp et al 2004[34]	MultiHance/Magnevist @ 1.5T	27	Significant ($P \leq .05$) preference for MultiHance for contrast enhancement, lesion-to-brain contrast, lesion delineation, internal lesion structure, and overall image preference; significantly ($P \leq .05$) greater lesion enhancement with MultiHance at all time points from 2 minutes after injection
Colosimo et al 2004[35]	MultiHance/Dotarem @ 1.5T	23	Significant ($P \leq .05$) preference for MultiHance for contrast enhancement, lesion-to-brain contrast, lesion delineation, internal lesion structure, and overall image preference; significantly ($P \leq .05$) greater lesion enhancement with MultiHance at all time points from 2 minutes after injection
Essig et al 2006[36]	MultiHance/Magnevist and Dotarem @ 1/1.5T	45	Significantly greater lesion-to-brain ratio ($P < .003$), contrast-to-noise ratio ($P < .03$), and percentage enhancement ($P < .0001$) noted by both readers for MultiHance at all time points from 2 minutes postcontrast; significant preference for MultiHance for lesion border delineation ($P < .004$), lesion internal morphology ($P < .008$), contrast enhancement ($P < .0001$), and diagnostic preference ($P < .0005$)
Maravilla et al 2006[37]	MultiHance/Magnevist @ 1.5T	151	Significantly ($P \leq .001$) higher overall reader preferences for MultiHance; significant ($P \leq .0001$) preference for MultiHance demonstrated for diagnostic information end points, percentage of lesion enhancement, and CNR
Rowley et al 2008[39]	MultiHance/Omniscan @ 1.5T	136	Significantly ($P \leq .0001$) higher overall reader preferences for MultiHance; highly significant ($P \leq .0001$, all readers) preference for MultiHance demonstrated for all qualitative end points and for CNR
Rumboldt et al 2009[40]	MultiHance/Magnevist @ 3T	46	Significantly ($P \leq .0001$) higher overall reader preferences for MultiHance; significant ($P \leq .001$) preference for lesion border delineation and enhancement with MultiHance-enhanced images; significantly ($P \leq .05$) higher lesion-to-background ratio, CNR, and percentage of lesion enhancement noted with MultiHance
Siedl et al 2012[41]	MultiHance/Gadavist @ 1.5T	122	Significantly ($P \leq .0001$) higher overall reader preferences for MultiHance; highly significant ($P \leq .0001$, all readers) preference for MultiHance demonstrated for all qualitative endpoints and for CNR

Note:—SE indicates spin echo.