

Table 1 Full summary of APT clinical studies published in 2003–2020

Title	Authors	Year	Study size	Stroke classification	Treatment received	Field strength	RF irradiation scheme	APT MRI acquisition scheme	APT MRI acquisition time	APT quantification method	Other MRI data acquired	Ref.
Saturation power dependence of amide proton transfer image contrasts in human brain tumors and strokes at 3 T	Zhao <i>et al.</i>	2011	4	(Acute) Average 4.3 ± 2.5 days after onset of stroke with a range of 1–7 days	Not stated if patients received treatment prior to imaging	3 T	500 ms off-resonance continuous-wave RF irradiation of power 1, 2, and 3 μ T	Single-slice turbo-spin-echo imaging readout with sensitivity-encoding factor of 2	Around 3 min	Magnetization transfer ratio asymmetry (MTR_{asym})	T ₂ -w, T ₁ -w, FLAIR, Gd-T ₁ -w	(38)
Assessment of ischemic penumbra in patients with hyperacute stroke using amide proton transfer (APT) chemical exchange saturation transfer (CEST) MRI	Tietze <i>et al.</i>	2014	10	(Hyperacute) 7 patients were imaged <4 h after onset of symptoms (average of 2 h 7 min \pm 1 h 7 min). 3 patients had more uncertain time of onset (between 1 and 24 h)	Only patients awaiting thrombectomy and patients found unsuitable for thrombolysis were included.	3 T	200 ms block RF irradiation of power 0.5 μ T	Three-dimensional gradient echo with a single shot turbo field echo (TFE) readout (TFE factor, 36)	3 min 20 s	Lorentzian difference analysis (LDA), and asymmetry analysis as the ratio of reference signal to APT signal	DWI, T ₂ FLAIR, DSC	(36)
Comparing different analysis methods for quantifying the MRI amide proton transfer (APT) effect in hyperacute stroke patients	Tee <i>et al.</i>	2014	6 [†]	(Hyperacute) Range of 1 h 43 min to 5 h 46 min	3 patients received intravenous tissue plasminogen activator during the MRI scan	3 T	50 Gaussian RF irradiation pulses; flip angle of 184°; duration of 20 ms; spacing of 20 ms; average power of 0.55 μ T	Single-slice spin-echo planar imaging readout	Around 3 min	MTR_{asym} , complementary MTR_{asym} , and multi-pool Bloch-McConnell model fitting (APTR*).	T ₁ , DWI	(26)
Identifying the ischaemic penumbra using pH-weighted magnetic resonance imaging	Harston <i>et al.</i>	2015	12 [†]	(Hyperacute) Range of 1 h 35 min to 11 h 6 min	4 patients received thrombolysis during scanning, 2 patients received thrombolysis prior to scanning	3 T	50 Gaussian RF irradiation pulses; flip angle of 184°; duration of 20 ms; spacing of 20 ms; average	Single-slice echo-planar imaging.	2 min 45 s	APTR*	DWI, T ₁ -w MP-RAGE, vessel-encoded pseudocontinuous ASL-PWI, T ₂ -w FLAIR	(33)

							power of 0.55 μ T					
Evolution of cerebral ischemia assessed by amide proton transfer-weighted MRI	Song <i>et al.</i>	2017	39	(Hyperacute-Acute) 4 patients were imaged ≤ 6 h; 18 patients, 6 h < onset time ≤ 48 h; 10 patients, 48 h < onset time ≤ 96 h, and 7 patients, 96 h < onset time ≤ 168 h	Patients receiving intravenous t-PA treatment and endovascular thrombectomy before APT scan were excluded	3 T	Not explicitly stated; two papers were cited for the CEST image acquisition protocol, but different saturation pulses were used in the papers cited (44,45)	Single-slice fat-suppressed, single-shot, turbo-spin-echo imaging with factor of 54	3 min 12 s	MTR _{asym}	DWI, T ₂ -w, T ₁ -w	(40)
Improving the detection sensitivity of pH-weighted amide proton transfer mri in acute stroke patients using extrapolated semisolid magnetization transfer reference signals	Heo <i>et al.</i>	2017	30	(Hyperacute) All imaged <7 h after onset of symptoms	Not stated if patients received treatment prior to imaging	3 T	Four block RF saturation pulses of duration 200 ms and amplitude of 2 μ T	Single-slice fat-suppressed, turbo spin-echo imaging with factor of 45	3 min 14 s	Quantitative APT [#] and NOE [#] using extrapolated semisolid magnetization transfer reference (EMR) analysis, MTR _{asym}	T ₂ -w FLAIR, GRE hemosiderin weighted sequence, TOF MR angiography, DWI, T ₂ *-w DSC	(37)
Depiction of acute stroke using 3-Tesla clinical amide proton transfer imaging: saturation time optimization using an <i>in vivo</i> rat stroke model, and a preliminary study in human	Park <i>et al.</i>	2017	1	(Acute) Patient imaged 4 days after acute middle cerebral artery infarction	Not stated if patient received treatment	3 T	Sinc-Gaussian pulse at B _{1,rms} amplitude of 1.2 μ T and 4 s saturation time	Three-dimensional turbo spin-echo imaging	2 min 30 s	MTR _{asym}	DWI	(39)

APT weighted MRI as an effective imaging protocol to predict clinical outcome after acute ischemic stroke	Lin <i>et al.</i>	2018	55	(Acute) 24–48 h from symptom onset	Patients receiving intravenous t-PA treatment before APT scan were excluded	3 T	50 Fermi MT saturation pulses with width of 40 ms, flip angle of 340°, duty cycle of 50%, and power of 1 μ T	Single-slice MT-prepared echo-planar imaging	Around 30 min	MTR _{asym}	DWI, T ₂ -w, T ₂ -w FLAIR	(29)
Amide Proton Transfer MRI Signal as a Surrogate Biomarker of Ischemic Stroke Recovery in Patients With Supportive Treatment	Yu <i>et al.</i>	2019	43	(Hyperacute-Early subacute) First scan on presentation ranged from 6h to 8 days from symptom onset. Follow-up scans ranged from 2–45 days	Patients scanned pre-treatment and after receiving supportive treatment, including antiplatelet and anticoagulation therapy, and free radical scavenging	3 T	Pseudocontinuous, off-resonance RF irradiation (saturation duration of 800 ms, power level of 2 μ T)	Single-slice single-shot, turbo-spin-echo readout with factor of 54	3 min 12 s	MTR _{asym}	DWI, T ₁ -w, T ₂ -w, FLAIR	(30)
Quantitative CEST imaging of amide proton transfer in acute ischaemic stroke	Msayib <i>et al.</i>	2019	12 [†]	(Hyperacute) Range of 1h 35min to 11h 6min	4 patients received thrombolysis during scanning, 2 patients received thrombolysis prior to scanning	3 T	50 Gaussian RF irradiation pulses; flip angle of 184°; duration of 20 ms; spacing of 20 ms; average power of 0.55 μ T	Single-slice spin-echo echo-planar imaging	2 min 45 s	MTR _{asym} , apparent APT (APT*), spillover-corrected MTR (MTR _{Rex}), post-acquisition LDA (paLDA), APTR*	DWI, T ₁ -w MP-RAGE, vessel-encoded pseudocontinuous ASL-PWI, T ₂ *-w FLAIR	(34)
Partial volume correction for quantitative CEST imaging of acute ischemic stroke	Msayib <i>et al.</i>	2019	12 [†]	(Hyperacute) Range of 1 h 35 min to 11 h 6 min	4 patients received thrombolysis during scanning, 2 patients received thrombolysis prior to scanning	3 T	50 Gaussian RF irradiation pulses; flip angle of 184°; duration of 20 ms; spacing of 20 ms; average power of 0.55 μ T	Single-slice spin-echo echo-planar imaging	2 min 45 s	APTR*	DWI, T ₁ -w MP-RAGE, vessel-encoded pseudocontinuous ASL-PWI, T ₂ -w FLAIR	(35)
Repeatability of amide proton transfer-weighted signals in the brain	Lee <i>et al.</i>	2020	12	(Acute-Early Subacute) Two initial scans ranging from 1.6–	Only patients considered unsuited	3 T	80 sinc-Gaussian off-resonance RF pulses of 50 ms	Three-dimensional turbo-spin-echo imaging	5 min 30 s	MTR _{asym}	T ₂ -w, DWI	(41)

according to clinical condition and anatomical location				8.4 days from symptom onset, and one more scan within 48h after the initial scans for repeatability analysis	for thrombolysis were included		pulse duration (4 s total duration) and power of 1.2 μ T					
Correlations of amide proton transfer-weighted MRI of cerebral infarction with clinico-radiological findings	Momosaka <i>et al.</i>	2020	29	(Hyperacute-Early Subacute) Range of 1.5–322 h after onset; median time after onset was 52.0 hours	Patients who received endovascular therapy for brain infarction before MRI were excluded	3 T	Saturation pulse of 2 s and 1.5 μ T power.	Single-slice turbo-spin-echo imaging.	2 min 20 s	MTR _{asym}	DWI, T ₁ -w, T ₂ -w, FLAIR, 3D TOF MR angiography	(43)
Novel proton exchange rate MRI presents unique contrast in brains of ischemic stroke patients	Wang <i>et al.</i>	2020	17	(Acute-Early Subacute) Range of 2–18 days	Not stated if patient received treatment	3 T	Saturation pulse of 1.5 s and 1.5, 2.5, and 3.5 μ T power	Single-slice spin-echo echo-planar imaging	3 min 18 s	Omega plot analysis, MTR _{asym}	T ₁ -FLAIR, T ₂ -FLAIR, DWI	(42)

[†]The studies by Harston *et al.* (33) and Msayib *et al.* (34,35) used data from the same patient cohort; Tee *et al.* (26) also had partial patient data overlap with the three studies.