Advancing Clinical and Neuroscientific Research Through Accessible and Optimized Protocol Design at 3T

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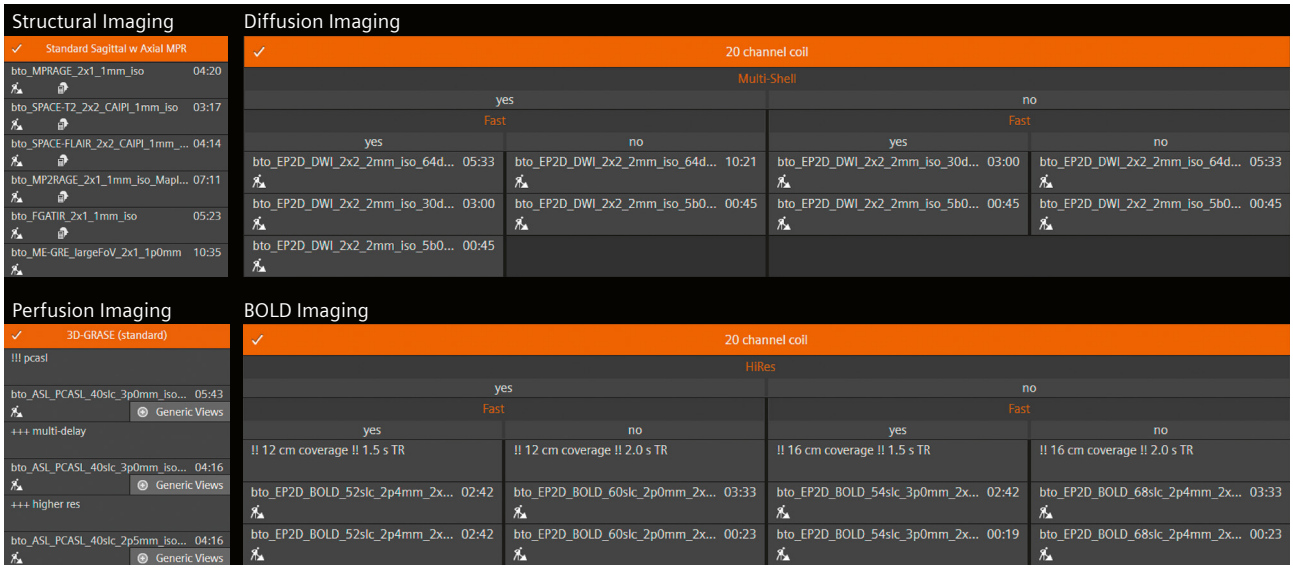
Background

Rising concern about healthcare costs and research funding is driving transformative shifts in the field of MR imaging. Collaborative efforts among academics, clinicians, and industry experts are helping dispel outdated notions of MRI as a slow and costly modality. Nevertheless, cutting-edge technological advancements achieved in academia and industry are difficult to translate into a shift in cognitive neuroscience and clinical research and patient care due to a multitude of factors – particularly the availability of technical expertise and time. Clinicians and neuroscientists often rely on colleagues and/or consortia (such as the Human Connectome Project and the Alzheimer's Disease Neuroimaging Initiative) to obtain imaging protocols for their research. This results in a wide variation in imaging protocols used within a single institution, and even by a single researcher for their different projects. Even sequences considered fairly routine and standard, such as T1w MPRAGE, have a large variation in imaging parameters, and there is no guarantee they will be compatible with post-hoc data analyses. In this article, we detail a strategic approach to developing a set of optimized neuroimaging protocols and present optimized parameters for the 3T MAGNETOM Prisma scanner (Siemens Healthcare, Erlangen, Germany) that are not only faster and more efficient but have also been tested and validated using community-standard MRI post-processing software.

Design principles

When optimizing the BRAIN-TO (Brain Research in Advanced Imaging and Neuromodeling – Toronto) protocols, several overarching principles were applied:



1 Example BTO imaging strategies laid out using the MAGNETOM Prisma Dot Cockpit interface.

First, the protocols should be built on product sequences from Siemens Healthineers (no work-in-progress packages or C2Ps) to maximize accessibility.

Second, all protocols should have spatially isotropic voxels to reduce partial voluming and voxel volumes. Because the cortex is curved, using anisotropic voxels (as is often the case in patient care) potentially reduces diagnostic value in the dimension with the lowest spatial resolution and should therefore be avoided.

Third, each scan should have a maximum acquisition time of 5 to 6 minutes (exceptions include multi-echo FLASH, multi-shell diffusion, resting-state, and functional MRI) to minimize participant discomfort and motion artifacts.

Fourth, the protocols should be optimized to take advantage of the acceleration capabilities of the head coil (20-channel Head/Neck, 32-channel Head, 64-channel Head/Neck), thus offering higher spatial and/or temporal resolution.

Finally, these optimized protocols should be organized using the Strategy and Decision Tree features in the Dot Cockpit interface from Siemens Healthineers. This means they will offer easy access to the end-users and can be made available to collaborating institutes as .exar1 packages. Unless otherwise specified, the parameters, data, and results illustrated hereafter are for the 20-channel Head/Neck coil.

BRAIN-TO (BTO) protocols

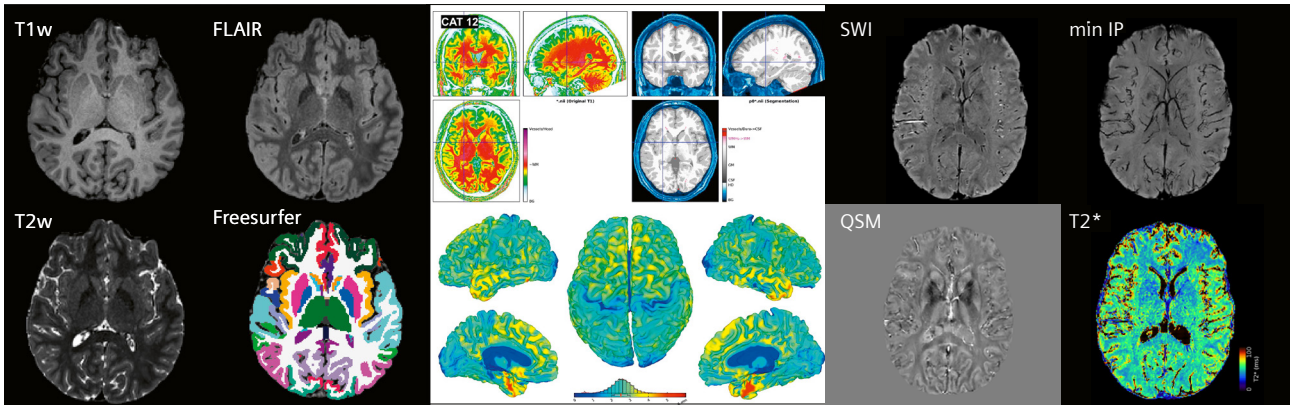
All data acquired from BTO protocols have been tested and validated for clinical and neuroscientific research applications using community-standard tools such as Freesurfer [1], FSL [2], SPM [3], CAT [4], and AFNI [5]. Generalized versions of the code and/or containers, as well as a wiki with recommendations for post-processing, are available through our lab at *https://github.com/BRAIN-TO/bto_mri_protocols_info*.

Structural imaging

In line with the design principles outlined earlier, the structural imaging component of the BRAIN-TO protocol set constitutes 1 mm isotropic 3D MPRAGE, 3D MP2RAGE, 3D SPACE T2, and 3D SPACE FLAIR sequences. A multi-echo FLASH protocol has also been incorporated. It enables quantitative T2* mapping, susceptibility weighted imaging (SWI) [6], and quantitative susceptibility mapping (QSM) [7] and takes about 10 minutes to acquire in 1 mm isotropic and high-resolution variants (only tested for 32- and 64-channel coils). It is important to point out that clinical research applications have different requirements to diagnostic imaging [8]. In this context, the increase in resolution and savings in time are a good trade-off [9] to enable resolution and field-of-view (FOV) matching of the T1w and FLAIR images and their integration into a post-processing pipeline without resampling artifacts.

	Sequence	Spatial resolution (mm)	Sequence parameters	Acquisition time (min:sec)	Acquisition time difference	Voxel volume difference
Typical T1w	3D MPRAGE	1 × 1 × 1	GRAPPA = 2, TE = 4.1 ms, TR = 2000 ms, IR = non-sel, TI = 899 ms, α = 8°, FOV = 256 × 256, 160 axial slices, Inline MPR = off	06:00		
BTO T1w	3D MPRAGE	1 × 1 × 1	GRAPPA = 2, TE = 2.88 ms, TR = 2100 ms, IR = non-sel, TI = 900 ms, α = 9°, FOV = 256 × 256, 256 sagittal slices, Inline MPR = tra	04:20	– 28%	0%
Typical FLAIR	IR 2D TSE	0.8 × 0.8 × 4	GRAPPA = 2, TE = 94 ms, TR = 9000 ms, TI = 2500 ms, IR = Slice-sel, α = 150°, FOV = 275 × 245, 32 axial slices, distance factor = 25%, Inline MPR = off, interpolation = on	02:44		
BTO FLAIR	3D SPACE	1 × 1 × 1	CAIPIRINHA = 2 × 2, TE = 393 ms, TR = 4500 ms, TI = 1800 ms, IR = non-sel, α = variable, FOV = 256 × 256, 256 sagittal slices, Inline MPR = tra	04:14	+ 55%	– 61%
BTO T1 map	3D MP2RAGE	1 × 1 × 1	GRAPPA = 2, TE = 2.98 ms, TR = 4500 ms, TI_1/TI_2 = 850/2550 ms, IR = non-sel, α_1/α_2 = 5°/6°, FOV = 256 × 256, 224 sagittal slices, distance Inline MPR = tra, MapIt = T1 map	07:11	+ 20%	0%
BTO multi-echo	3D GRE	1 × 1 × 1	GRAPPA = 2, $TE_{1\text{-}3}$ = 12/24/38 ms, TR = 55 ms, α = 20°, FOV = 224 × 224, 160 axial slices	10:35		

Table 1: Comparison of typical vs. BTO protocols for structural imaging



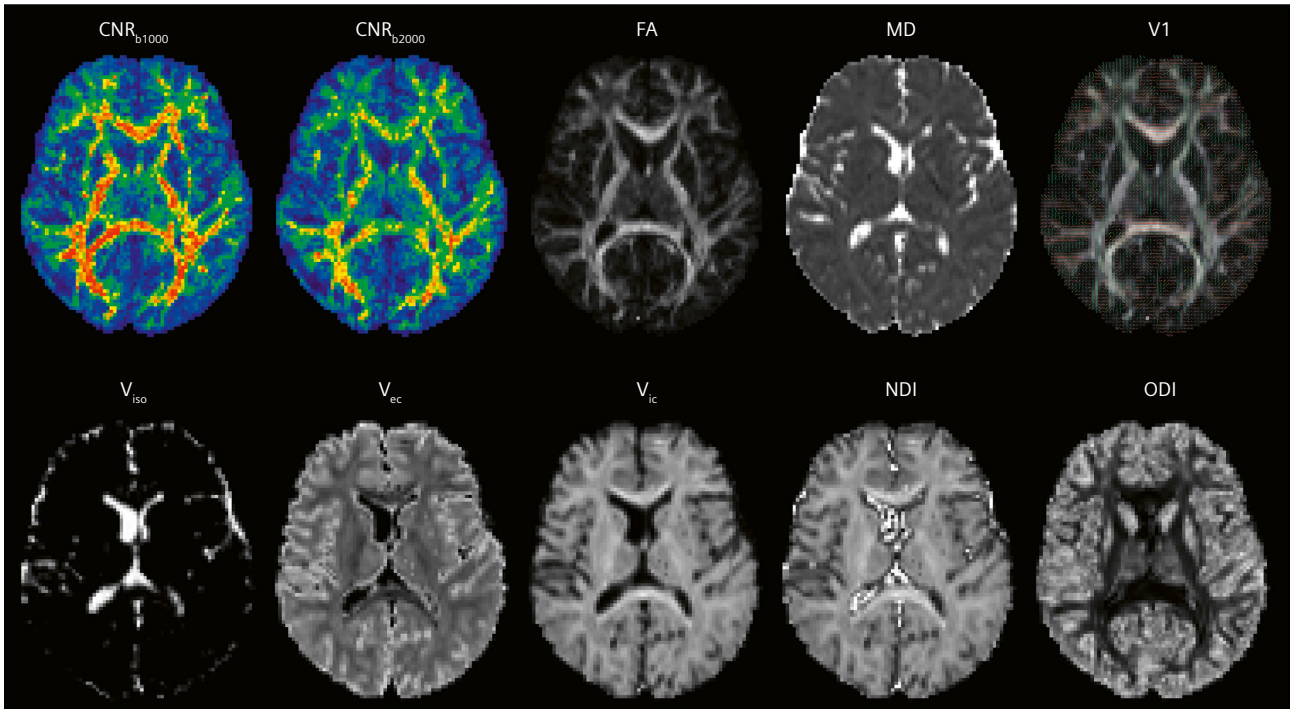
2 Example images from the BTO structural protocols and their post-processed results.

Diffusion imaging

The diffusion imaging component consists of a fast single-shell protocol, a comprehensive single-shell protocol, and a multi-shell protocol for neurite orientation dispersion density imaging (NODDI) [10]. Each protocol has been implemented with two versions: first, with the default diffusion vector set from Siemens Healthineers; second, with a custom diffusion vector set with interspersed b0s while ensuring uniform coverage of q-space [11]. The data acquired from BTO protocols were tested, processed, and evaluated for quality using community-standard tools such as FSL and MRtrix3 [12]. Two example scenarios can be envisioned here. In the first, the investigator is only interested in assessing fractional anisotropy (FA), mean diffusivity (MD), and diffusion tensor (DTI). In that case, they can opt for the BTO single-shell, fast protocol to acquire the data in 3 minutes. In the second scenario, the researcher is also interested in tractography, and can opt for the BTO single-shell protocol to acquire the data in 5.5 minutes. The end-user can make these decisions with the knowledge that the data will be of sufficient quality during

	Sequence	Spatial resolution (mm)	Sequence parameters	Acquisition time (min:sec)	Acquisition time difference	Voxel volume difference
Typical DWI	2D EPI	2.4 × 2.4 × 2.4	GRAPPA = 2, SMS = 2, TE = 68 ms, TR = 3400 ms, Partial Fourier = 6/8, FOV = 230 × 230, echo-spacing = 0.76 ms, bandwidth = 1488 Hz/px, 68 axial slices, diff. directions = 64, b_1/b_2 = 0/1000 s/mm², averages b_1/b_2 = 1/2	07:37		
BTO DWI (single-shell)	2D EPI	2 × 2 × 2	GRAPPA = 2, SMS = 2, TE = 75 ms, TR = 4500 ms, Partial Fourier = 6/8, FOV = 220 × 220, echo-spacing = 0.56 ms, bandwidth = 2164 Hz/px, 84 axial slices, diff. directions = 64, b_1/b_2 = 0/1000 s/mm², averages b_1/b_2 = 5/1	05:33	– 27%	– 42%
BTO DWI (single-shell, fast)	2D EPI	2 × 2 × 2	GRAPPA = 2, SMS = 2, TE = 75 ms, TR = 4500 ms, Partial Fourier = 6/8, FOV = 220 × 220, echo-spacing = 0.56 ms, bandwidth = 2164 Hz/px, 84 axial slices, diff. directions = 30, b_1/b_2 = 0/1000 s/mm², averages b_1/b_2 = 5/1	03:00	– 61%	– 42%
BTO NODDI (multi-shell)	2D EPI	2 × 2 × 2	GRAPPA = 2, SMS = 2, TE = 75 ms, TR = 4500 ms, Partial Fourier = 6/8, FOV = 220 × 220, echo-spacing = 0.56 ms, bandwidth = 2164 Hz/px, 84 axial slices, diff. directions = 30/64, b_1/b_2 = 0/1000/2000 s/mm², averages b_1/b_2 = 5/1/1	08:33 **As 2 runs** Run 1: 30 dirs, b1000 = 03:00 Run 2: 64 dirs, b2000 = 5:33	+ 12%	– 42%

Table 2: Comparison of typical vs. BTO protocols for diffusion imaging



3 Example images from the BTO diffusion NODDI protocol and its post-processed results.

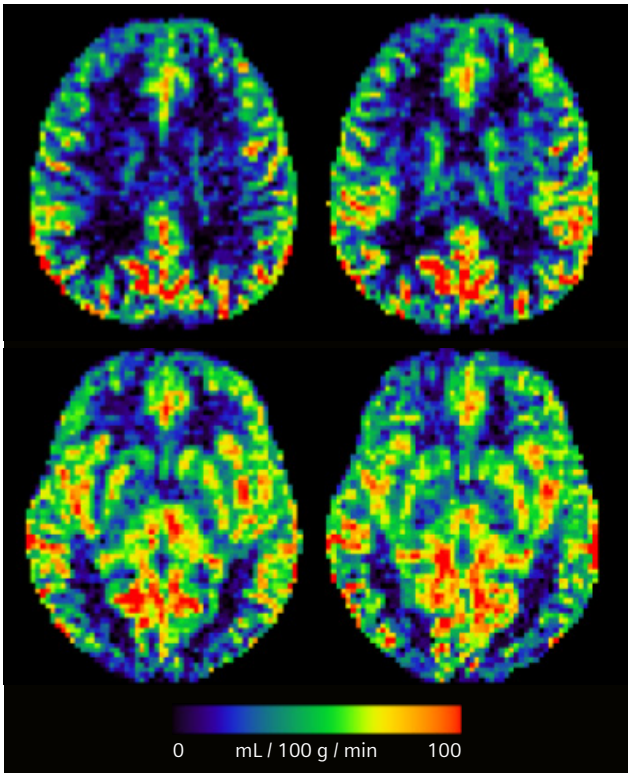
post-processing. It is important to reiterate that these are optimized, general-purpose protocols. They are not designed for bespoke investigations.

Perfusion imaging

Non-invasive perfusion MRI is typically carried out using Arterial Spin Labelling (ASL) sequences that use magnetically labelled arterial blood water as an endogenous tracer to measure blood flow. While community-standard protocols [13] with spatial resolutions of 3 to 4 mm in-plane and 4 to 8 mm slice thickness may suffice for detecting macroscale perfusion patterns in the brain, the anisotropicity and increased partial voluming is sub-optimal for clinical and neuroscientific research. The BTO perfusion protocol set consists of whole-brain 3 mm and 2.5 mm isotropic pseudocontinuous ASL (pCASL) and pulsed ASL (PASL) options in a total acquisition time of 4 to 6 minutes. Recently, we pushed this boundary further to evaluate the feasibility of 2 mm isotropic whole-brain ASL and the impact of coil and post-processing choices on the perfusion maps [14].

BOLD imaging (functional MRI)

The functional MRI (fMRI) component that uses the gradient-echo 2D EPI sequence from Siemens Healthineers

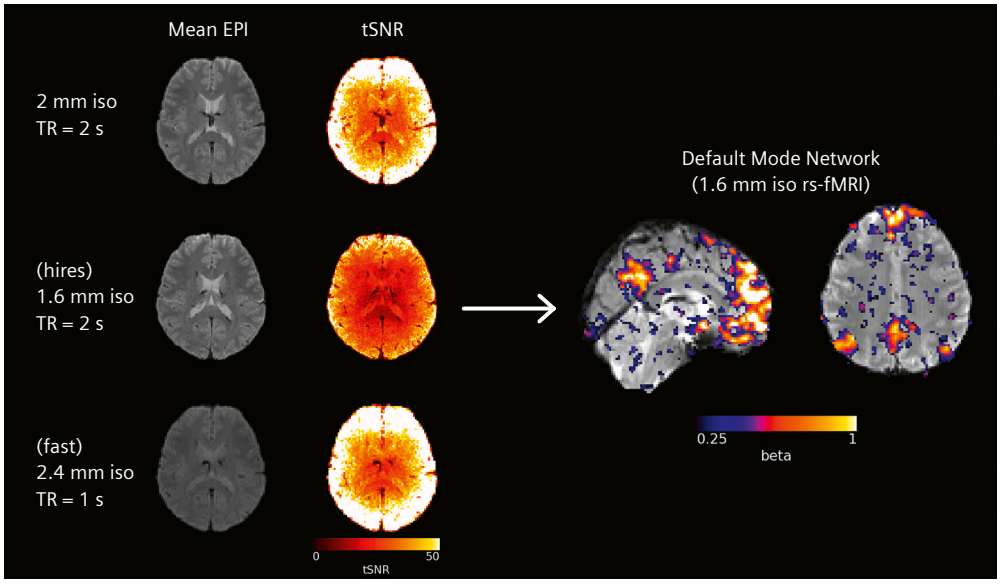


4 Example slices of a single-subject cerebral blood flow map from the BTO 2.5 mm isotropic perfusion protocol.

is by far the most diverse component of the BTO protocol set. Particular emphasis has been placed on providing investigators with a modern fMRI protocol with 2.4 mm isotropic resolution and a community-standard TR of 2.0 seconds employing nominal acceleration factors and applicable for any coil. All BTO fMRI protocols have dedicated variants for 32- and 64-channel coils to make maximum use of the acceleration capabilities. This results in particularly high in-plane resolution and/or Simultaneous Multi-Slice (SMS) factors for higher temporal resolution. For example, the 64-channel coil variant of the standard BTO BOLD protocol has an increased SMS factor of 4 and a volume TR of 1 second for the same spatial resolution. While staying true to the design principles and generalizability, the BTO BOLD protocols also offer direct decision-making choices without having to worry about the implications of the other parameter choices, as we have assessed the protocols using both resting and task fMRI. We are delighted to report that, over the past year, our protocol offerings have covered a vast array of requirements at our site and did not require case-by-case modifications.

	Sequence	Spatial resolution (mm)	Sequence parameters	Acquisition time (min:sec)	Acquisition time difference	Voxel volume difference
Typical BOLD	2D EPI	3 × 3 × 4	GRAPPA = 2, TE = 30 ms, α = 85°, FOV = 220 × 220, echo-spacing = 0.93 ms, bandwidth = 1184 Hz/px, 40 axial slices	2.0		
BTO BOLD (std)	2D EPI	2.4 × 2.4 × 2.4	GRAPPA = 2, SMS = 2, TE = 30 ms, α = 70°, FOV = 220 × 220, echo-spacing = 0.49 ms, bandwidth = 2470 Hz/px, 68 axial slices	2.0		– 62%
BTO BOLD (std high-res)	2D EPI	2 × 2 × 2	GRAPPA = 2, SMS = 2, TE = 30 ms, α = 70°, FOV = 220 × 220, echo-spacing = 0.53 ms, bandwidth = 2272 Hz/px, 62 axial slices	2.0		– 78%
			32- / 64-channel coils			
BTO BOLD (high-res)	2D EPI	1.6 × 1.6 × 1.6	RAPPA = 2, SMS = 4, TE = 30 ms, α = 70°, FOV = 220 × 220, echo-spacing = 0.61 ms, bandwidth = 1906 Hz/px, 100 axial slices	2.0		– 88%
BTO BOLD (fast)	2D EPI	2.4 × 2.4 × 2.4	GRAPPA = 2, SMS = 4, TE = 30 ms, α = 70°, FOV = 220 × 220, echo-spacing = 0.49 ms, bandwidth = 2470 Hz/px, 68 axial slices	1.0	– 50%	– 62%

Table 3: Comparison of typical vs. BTO protocols for BOLD imaging



5 Example slices of the mean EPI images and temporal signal-to-noise ratio (tSNR) of three BTO BOLD fMRI protocols acquired using the 32-channel Head coil. Illustration of the Default Mode Network obtained from a high-resolution (hi-res) 1.6 mm isotropic resting-state BOLD fMRI acquisition.

Summary

The BRAIN-TO (BTO) protocols present a comprehensive approach to making optimized neuroimaging protocols accessible to clinical and neuroscientific researchers. The BTO protocols are designed based on key principles, utilizing Siemens Healthineers product sequences for accessibility. They incorporate spatially isotropic voxels, efficient scan times, and dedicated variants for using head coils with denser coil arrays. We hold Town Hall sessions to disseminate information about the BTO protocols to our on-site neuroimaging community. To improve the accessibility to advanced neuroimaging, we make the guidelines for processing data acquired with the standard protocols and analysis code available through a dedicated GitHub repository (*https://github.com/BRAIN-TO/bto_mri_protocols_info*). The BTO protocols not only cover diverse imaging modalities, including structural imaging, diffusion imaging, perfusion, and BOLD imaging, but have also been rigorously tested and validated using community-standard post-processing tools. This enhances their reliability, reassures the end-user, and makes cutting-edge plug-and-play neuroimaging a reality.

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