Major aspects of the VBM12 segmentation are:

1. **AMAP Segmenation** The segmentation approach is based on an Adaptive Maximum A Posterior (AMAP) technique without the need for a priori information about tissue probabilities. That is, the Tissue Probability Maps (TPM) are not used constantly in the sense of the classical Unified Segmentation approach (Ashburner et. al. 2005), but only for spatial normalization and the initial skull-stripping. The following AMAP estimation is adaptive in the sense that local variations of the parameters (i.e., means and variance) are modeled as slowly varying spatial functions (Rajapakse et al. 1997). This not only accounts for intensity inhomogeneities but also for other local variations of intensity.
2. **Mixed Model** Additionally, the segmentation approach uses a Partial Volume Estimation (PVE) with a simplified mixed model of at most two tissue types (Tohka et al. 2004). We start with an initial segmentation into three pure classes: gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) based on the above described AMAP estimation. The initial segmentation is followed by a PVE of two additional mixed classes: GM-WM and GM-CSF. This results in an estimation of the amount (or fraction) of each pure tissue type present in every voxel (as single voxels - given by their size - probably contain more than one tissue type) and thus provides a more accurate segmentation.
3. **Noise Filter** Furthermore, we apply three denoising methods. The first method is an block-wise adaptive Non-Local Means (SANLM) denoising filter (Manjon et al. 2010). After global intensity correction an block-wise optimized non-local means (ORNLM) denoising filter is applied (Coupe et al. 2008). These filters remove noise while preserving edges and are implemented as preprocessing step. The third method is a classical Markov Random Field (MRF) approach, which incorporates spatial prior information of adjacent voxels into the segmentation estimation (Rajapakse et al. 1997) and is part of the AMAP segmentation. The strength of the ORNLM and MRF filter are automatically obtained by estimating the remaining noise in the image.
4. **Dartel Normalisation** Another important extension to the SPM12 segmentation is the integration of the Dartel normalisation (Ashburner 2007) into the toolbox by an already existing Dartel template in MNI space. This template was derived from 555 healthy control subjects of the IXI-database (http://www.brain-development.org) and provides the six Dartel iterations. Thus, for the majority of studies the creation of sample-specific Dartel templates is not necessary anymore.
5. **Local Adaptive Segmentation (LAS)** Beside WM-inhomogeneities, also the GM intensity can vary for different regions like the motor cortex, the basal ganglia, or in the occipital lobe. Although, these changes have an anatomical background, they depend on the MR-protocol and often lead to WM-overestimations for higher intensities and CSF-overestimations for lower intensities. Therefore, a local intensity transformation of all tissue classes is used to reduce this effects in the m*-image before the final AMAP segmentation. The strength of the changes is controlled by the LASstr parameter, with 0 for no LAS, small values (0.01-0.5) for small adaptations, 0.5 for average adaptations (default), and higher values (0.5-1)

for strong adaptations.

6. **Skull-Stripping** VBM12 contains a revised graph-cut based skull-stripping with a arbitrary strength, with 0 for a more liberal and wider brain masks and 1 for a more aggressive skull-stripping. The default is 0.5 and was successfully tested on a variety of different images. The strength parameter affects multiple internal parameters:

   - Intensity thresholds to deal with blood-vessels and meninges
   - Distance and growing parameters for the graph-cut/region-growing
   - Closing parameters that fill the sulci
   - Smoothing parameters that allow sharper or wider results

   If your segmentations still contain skull and other non-brain tissue (e.g. dura) you can try to increase the strength. If parts of the brain are missing in the segmentations the strength can be decreased.

7. **Cleanup** VBM12 includes a new cleanup routine that uses morphological, distance and smoothing operations to remove reminding meninges from the final segmentation. The strength of the cleanup is controlled by the cleanupstr parameter, with 0 for no cleanup, low values <0.5 for light cleanup, 0.5 for average cleanup (default), and 1 for strong cleanup.