PET HARMONIZATION TOOLBOX

USER MANUAL

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V1.0.0.beta - Mauro Namías - mnamias@gmail.com

The objective of this document is to provide instructions to perform quantitative harmonization experiments and processing on PET scanners by following the method published on the paper "A novel approach for quantitative harmonization in PET" by M. Namías *et. al.*, PMB 2018.

The aim of this toolbox is to determine the optimal reconstruction settings (post-filter) and minimum acquisition time to comply with EARL specifications (http://earl.eanm.org/cms/website.php?id=/en/projects/fdg_pet_ct_accreditation/accreditation_specifications.htm), by using cylindrical phantom acquisitions only.

Notice that this method and its results *does not replace* the accreditation provided by EANM/EARL. This toolbox is provided *as is* with no warranty of the results. Please read the licence.txt file before using.

1. INSTALLATION

Download the source code from https://github.com/mnamias/PET_Harmonization_Toolbox/releases
Copy it to the desired folder.

Start MATLAB

Run the function harmonization_toolbox.m. It will add the subfolders to the path.

2. PRELIMINARY REQUIREMENTS

Please update the PET scanner calibration files:

- Detector gains
- Energy tables
- Position maps
- Coincidence timing

Update normalization tables (usually performed with a cylindrical phantom filled with 18F or 68Ge, also called crystal efficiency on some scanners) and absolute activity calibration (also called well-counter cross calibration on some scanners) to ensure optimal scanner performance / image quality during the experiments.

Also check the dose calibrator accuracy for F18 and the synchronization of the dose calibrator and scanner console clocks. Accuracy should be better than 5%, ideally under 2%.

3. PHANTOM PREPARATION AND ACQUISITION

Materials

You will need:

- A fillable cylindrical phantom (NEMA 1994 phantom or similar) with 20 cm diameter. It is usually included with the PET system for routine calibration and QA.
- Ideally, a phantom holder (usually comes with the scanner). The phantom should be positioned on the holder and not on the scanner bed if possible. Philips scanners usually don´t allow to use the holders outside calibration mode.
- 70 MBq of 18F-FDG
- Dose calibrator (18F).
- Syringes, needles, Personal Protective Equipment (PPE), personal dosimeters, etc.
- Bubble level (spirit level).

Phantom Preparation and Image Acquisition

Phantom preparation.

- Measure the internal phantom volume. The typical NEMA NU-1994 phantom volume is 5640 ml.
- Calibrate 70 MBq of 18F-FDG (DO NOT USE 18F-FNa!) in a syringe.
- Activity =................................ MBq specified or calibrated at .... (hh:mm:ss)
- The reference time for the activity should be the estimated start of the PET acquisition. This means that there should be 70 MBq in the phantom at the time of the image acquisition. Register activity and measurement time.
- Fill the cylindrical phantom with distilled water. Remove 300-500 ml of water to be able to homogenize the activity.
- Add the activity into the phantom. Shake thoroughly to homogenize the activity. Fill the remaining volume and shake again. Leave no air bubbles.
- Measure residual activity. Activity = ... (MBq) measured at .... (hh:mm:ss)

Phantom positioning

- If available, place the phantom on the phantom holder.
- Level the phantom with the help of the bubble level and the phantom holder.
- Align the phantom with the help of the positioning lasers.
- The phantom should be centered on the FOV, both vertically and horizontally.
- Verify that the phantom is leveled with the help of scout images. The following picture shows an example of bad phantom leveling:

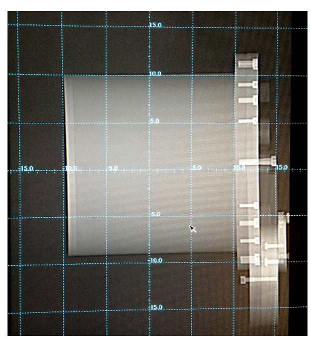
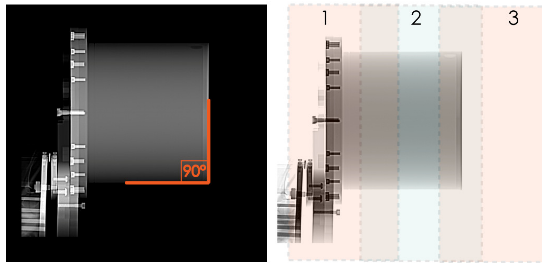


Image Acquisition

- Setup a PET/CT acquisition as usually done in clinical practice.
- Fill the injected and remaining activities (with their respective measurement times) on the scanner console.
- Setup two or three overlapping PET bed positions (use the default slice overlap used in the clinical protocols). 50 % overlap is the recommended value for normal axial FOV scanners (around 16 cm) with full acceptance angle, as it results in more uniform noise and resolution. Typical overlap values for large axial FOV scanners (Siemens TrueV, GE Discovery IQ, etc.) are lower than 50% since they use limited acceptance angles.

- The upper edge of the phantom (the one opposite to the holder) should be exactly in the center of the overlap region (between bed positions 2 and 3 or 1 and 2):



- Use the default CT protocol for attenuation correction. ^{68}Ge sources can also be used in stand-alone PET scanners.
- Acquisition time per PET bed: 20 minutes.
- Register the exact time of the PET acquisition start.
- Reconstruction settings: use the typical clinical recon settings and also setup an additional reconstruction **without any type of filtering (if available)**. Be sure to enable all quantitative corrections (attenuation, scatter, randoms, dead time, decay, normalization, etc.).
- Store the PET RAW data and CTAC series for future reconstructions if possible.
- Export all images in DICOM 3.0 format without compression, ideally from the scanner console.

Expected results

Image uniformity should be better than 10% for every slice and SUV errors should be under 5% for every slice (ideally under 3%). This functionality is not currently provided by the toolbox.

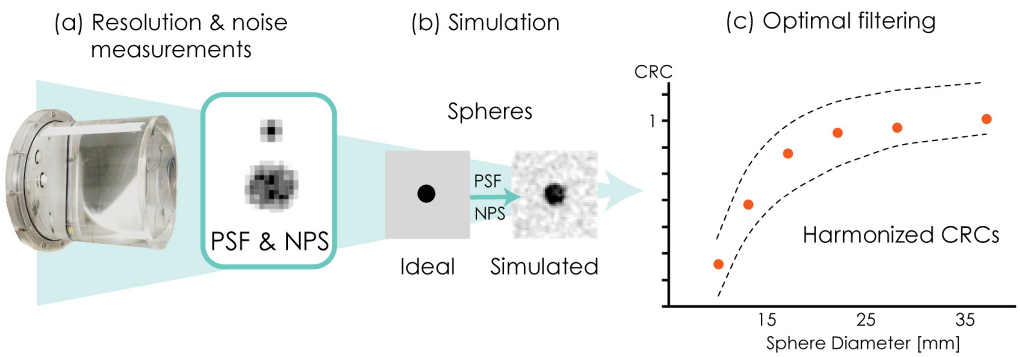
4. IMAGE PROCESSING

Materials

You will need:

- The (uncompressed) DICOM files of the cylindrical phantom. The files exported from the scanner console are usually uncompressed.
- The Harmonization Toolbox GUI (MATLAB software).

The overall workflow is as follows:

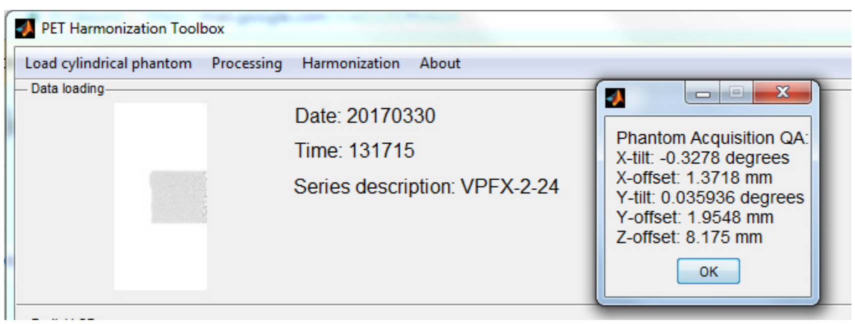


First, the resolution and noise power spectrum are estimated from the cylindrical phantom. This information is then used to simulate spheres that are used to estimate CRC values.

Image analysis

Image loading

- Open the Harmonization Toolbox GUI: (type: harmonization_toolbox)
- Select "Load cylindrical phantom" from the menu.
- Select the directory containing the DICOM files of the cylindrical phantom.
- The software will load the slices and perform a quality check to assess the positioning of the phantom. Currently, this is for informative purposes only.
- The toolbox will show the following information:

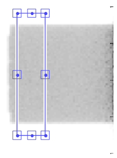


The date and time of the acquisition is shown, together with the series description. The message box shows the X&Y tilt and offsets and the Z-offset of the phantom. The X&Y offsets are the distances between the center of the phantom and the center of the PET FOV. The tilts are the angles between the phantom axis and the PET axis. The Z-offset is the distance between the top edge of the phantom and the center of the overlapping region of the PET FOVs.

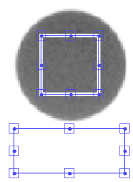
Image Processing

There are two options: manual and automatic processing. In automatic processing, the regions of interest to extract resolution and NPS estimates are automatically determined. *This mode is suitable for all users.* Under manual processing, the regions of interest are selected by the user and requires knowledge of the underlying method. The manual mode can be useful for special cases where some regions of the phantom should be avoided.

Manual radial LSF processing:

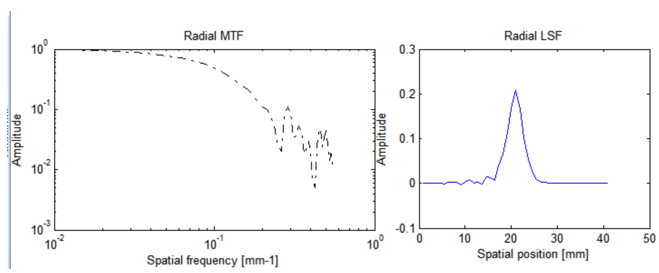


- Select an axial range close to the top edge of the phantom.
- Double click to continue.

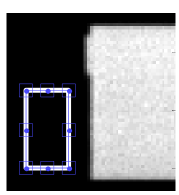


- Drag and select an ROI for the background, close to the active part of the phantom.
- Double click to accept.
- Drag and select an ROI for the foreground.
- Double click to accept.

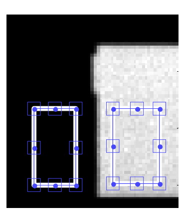
The radial LSF and MTF appear on the main screen of the GUI:



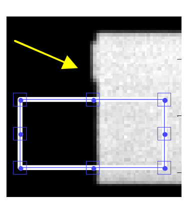
Manual axial LSF processing:



- Select an ROI representative of the background.
- Double click to continue.

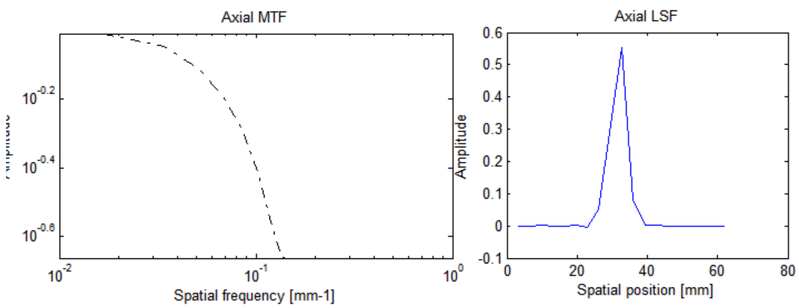


- Select an ROI representative of the background.
- Double click to continue.

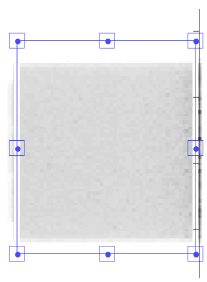


- Select an ROI representative of the saggital analysis range. ***Avoid*** holes in the top of the phantom if present (yellow arrow).
- Double click to continue.

The axial LSF and MTF appear on the main screen of the GUI:

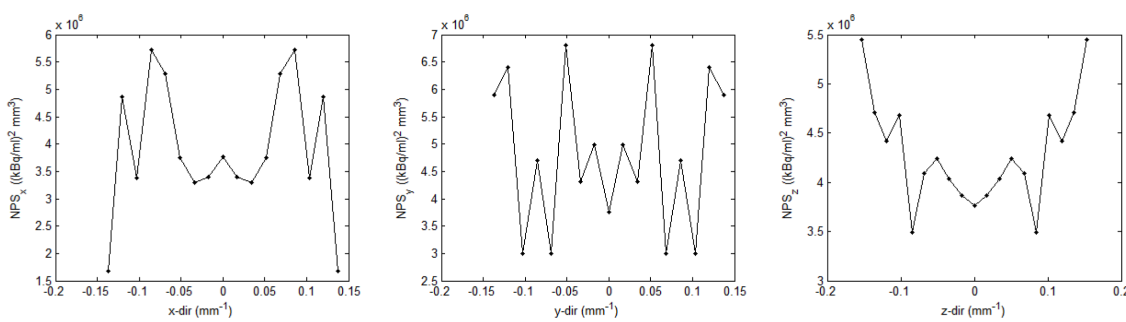


Manual NPS processing:



- Select the whole active axial range of the phantom.
- Double click to continue.

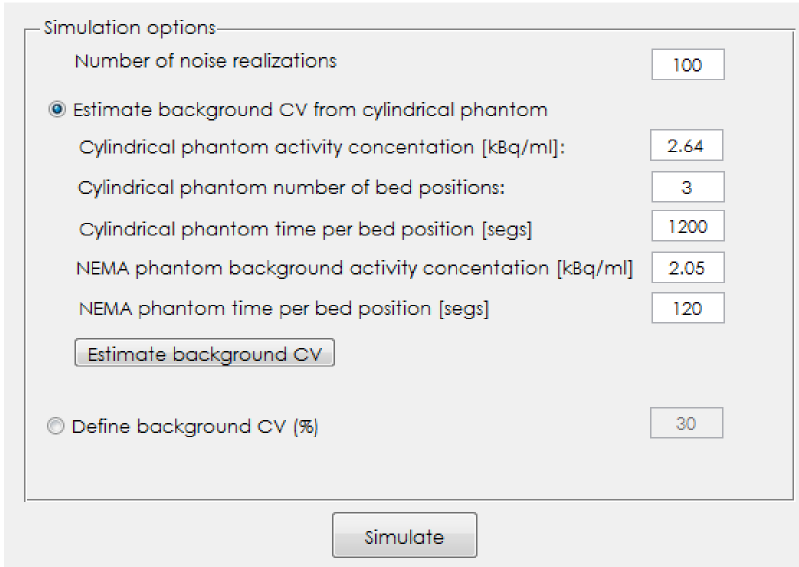
Three 1-D profile along the main frequency axis will be shown on the main GUI:



5. SIMULATION

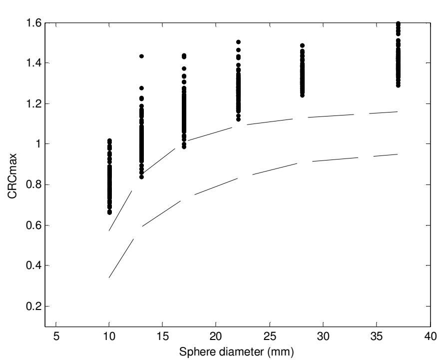
Once the radial and axial LSFs and the NPS are estimated, the spheres can be simulated.

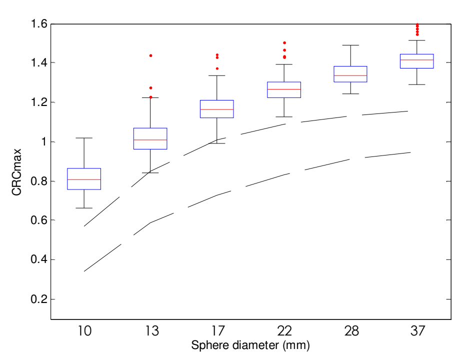
Select *Harmonization →Simulate spheres* from the main menu. A pop-up screen will appear:

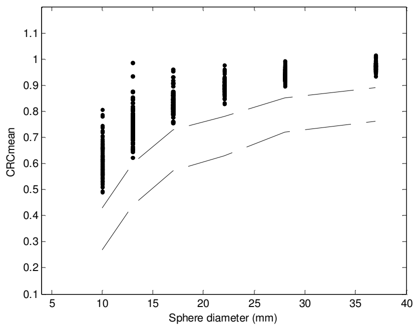


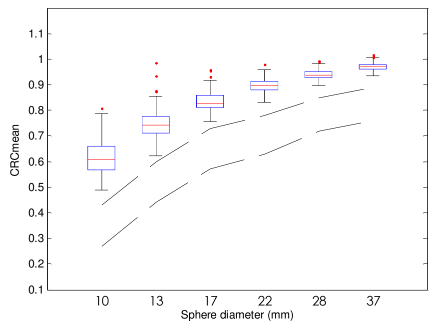
1. Select the number of noise realizations (default: 100). As the number of noise realizations increases, so does the sampling of the CRC distribution but at the expense of slower processing times.
2. The background CV of the simulated NEMA phantom can be estimated from the cylindrical phantom (default) or can be set to an arbitrary value. If the first option is desired:
    a. Check that the information from the cylindrical phantom is correct (activity concentration, number of bed positions and time per bed).
    b. Select the parameters of the NEMA phantom to be simulated. Activity and time can be changed.
    c. Click "Estimate background CV". The estimated value will replace the lower left edit box value.
3. Click "Simulate". The simulation can take a few minutes depending on the number of noise realizations.

The simulated CRCs appear on pop-up figures, both as scatter-plots and box-plots:



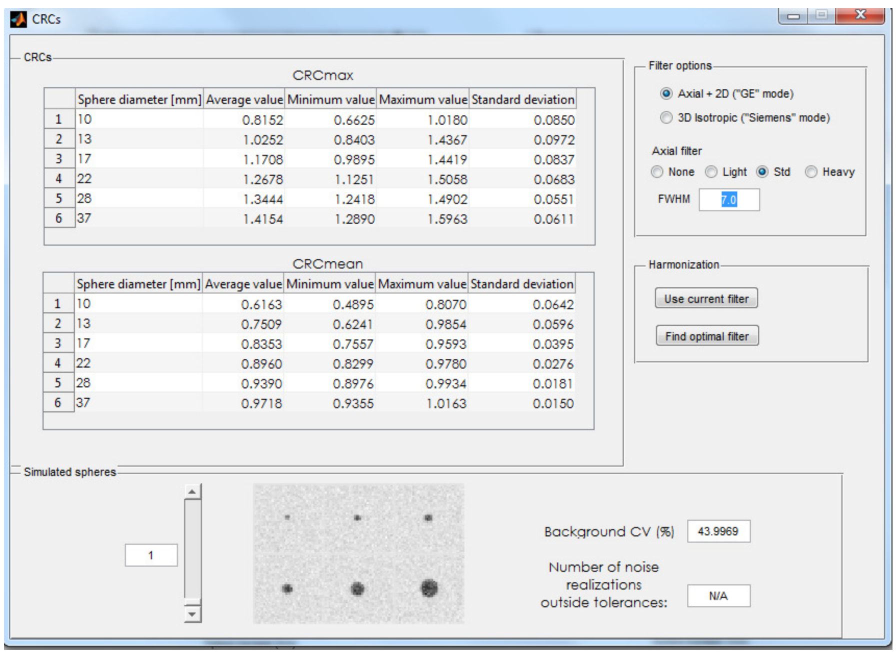






Notice that the demo phantom is **unfiltered**, so the CRC values are outside the EARL specifications.

The CRC analysis windows also appears, showing the results in a tabular way:



CRCmax

	Sphere diameter [mm]	Average value	Minimum value	Maximum value	Standard deviation
1	10	0.8152	0.6625	1.0180	0.0850
2	13	1.0252	0.8403	1.4367	0.0972
3	17	1.1708	0.9895	1.4419	0.0837
4	22	1.2678	1.1251	1.5058	0.0683
5	28	1.3444	1.2418	1.4902	0.0551
6	37	1.4154	1.2890	1.5963	0.0611

CRCmean

	Sphere diameter [mm]	Average value	Minimum value	Maximum value	Standard deviation
1	10	0.6163	0.4895	0.8070	0.0642
2	13	0.7509	0.6241	0.9854	0.0596
3	17	0.8353	0.7557	0.9593	0.0395
4	22	0.8960	0.8299	0.9780	0.0276
5	28	0.9390	0.8976	0.9934	0.0181
6	37	0.9718	0.9355	1.0163	0.0150

Under the "Simulated spheres" panel, all the noise realizations can be visualized with the slider control.

6. HARMONIZATION

There are two options to harmonize the CRC values:

1) Manual search of the optimal filter parameters.

The filter settings can be manually changed in the "Filter options" panel. Two modes are available:

- "GE" mode: a 2D filter + an axial filter are used. The axial filter can have the following settings:
  - None [0 1 0]

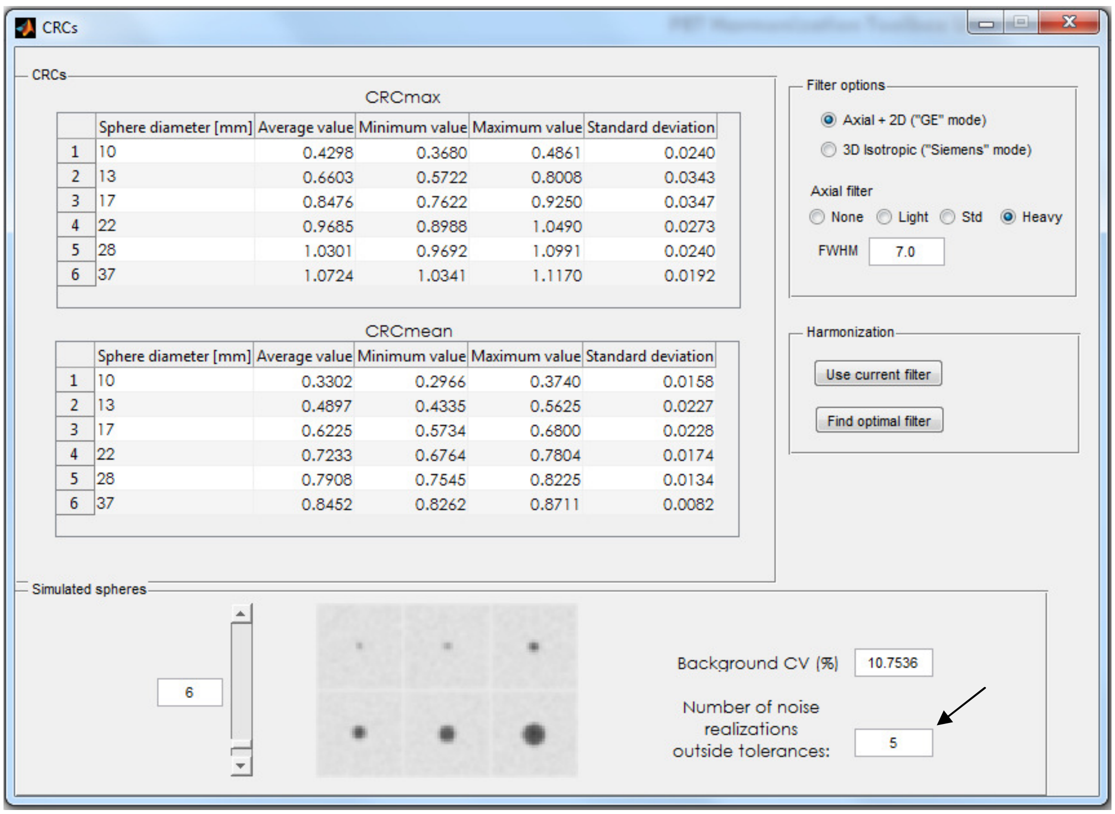
- Light [1 6 1]
- Standard [1 4 1]
- Heavy [1 2 1]

- "Siemens" mode: a 3D Gaussian isotropic filter is used.

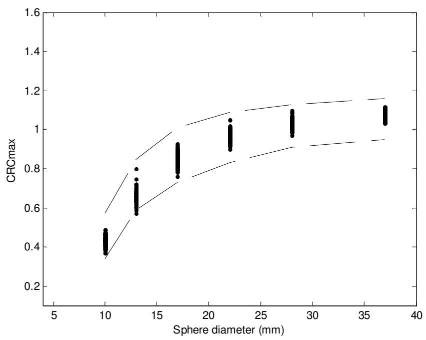
In "GE" mode, the "FWHM" edit box represents the 2D filter FWHM. In "Siemens" mode, the "FWHM" value represents the 3D FWHM value of the filter.

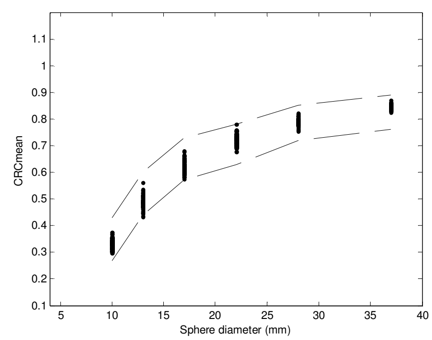
1. Select the mode (GE or Siemens).
2. If GE was selected, select the axial filter strength.
3. Select the FWHM value (in mm).
4. Press the "Use current filter" button.

New CRC figures appear, and the table is updated. The new background value is also shown:



Finally, the number of noise realizations outside tolerances are shown on the lower right of the screen.





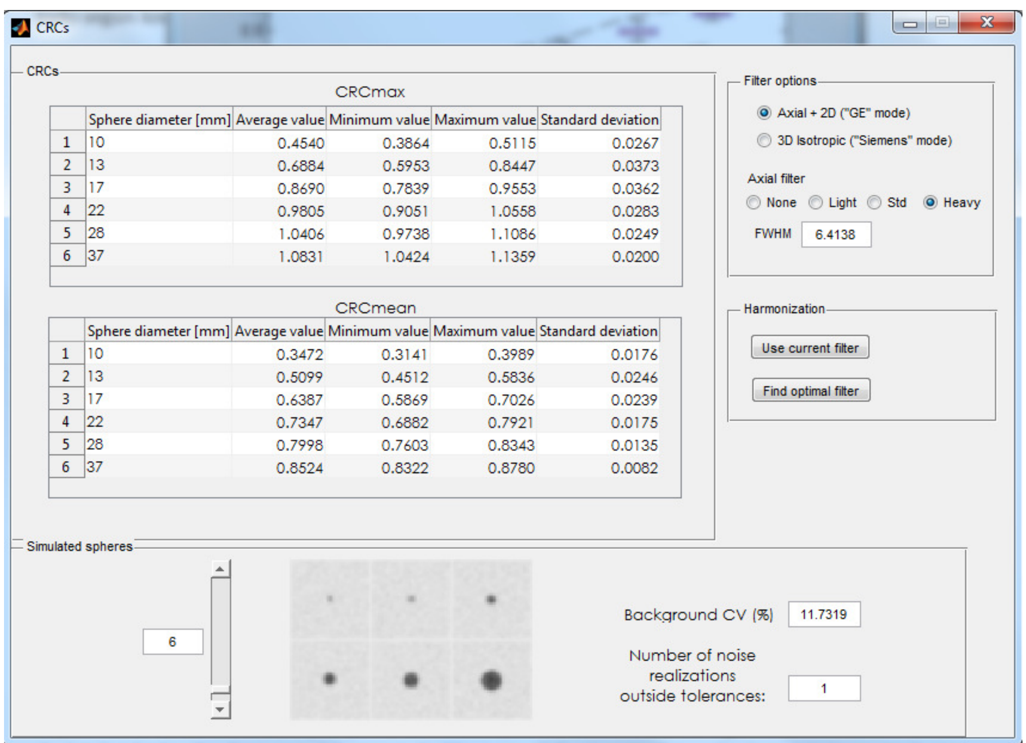
2) Filter optimization

The filter mode should be set before using the filter optimization routine since it doesn´t change the axial filter (i.e.: it only optimizes the 2D filter in "GE" mode).

1. Select the mode (GE or Siemens).
2. If GE was selected, select the axial filter strength.
3. Press the "Find optimal filter" button.

Please be patient, the optimization process can take a few minutes.

The new results after optimization are shown on the GUI:

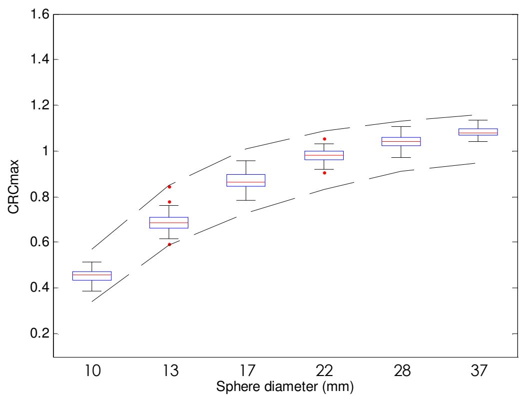


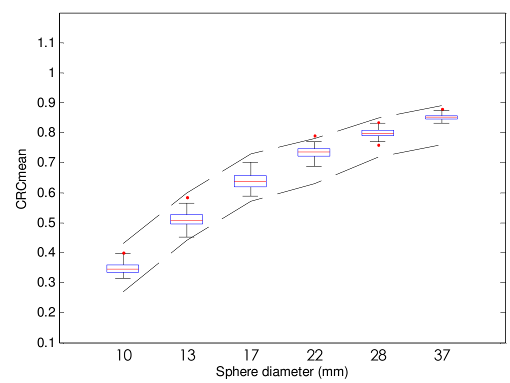
CRCmax

	Sphere diameter [mm]	Average value	Minimum value	Maximum value	Standard deviation
1	10	0.4540	0.3864	0.5115	0.0267
2	13	0.6884	0.5953	0.8447	0.0373
3	17	0.8690	0.7839	0.9553	0.0362
4	22	0.9805	0.9051	1.0558	0.0283
5	28	1.0406	0.9738	1.1086	0.0249
6	37	1.0831	1.0424	1.1359	0.0200

CRCmean

	Sphere diameter [mm]	Average value	Minimum value	Maximum value	Standard deviation
1	10	0.3472	0.3141	0.3989	0.0176
2	13	0.5099	0.4512	0.5836	0.0246
3	17	0.6387	0.5869	0.7026	0.0239
4	22	0.7347	0.6882	0.7921	0.0175
5	28	0.7998	0.7603	0.8343	0.0135
6	37	0.8524	0.8322	0.8780	0.0082





Sometimes it´s impossible to achieve perfect harmonization (i.e.: number of noise realizations outside tolerances = 0). Keep in mind that the EARL tolerances were designed for the mean values and not for a particular noise realization.

The filter settings that provide harmonized CRC values are the ones that should be set on the scanner console.