User guidelines for the T2*- estimation MATLAB Tool

General information

The tool consists of 2 components:

1. temporal voxel-by-voxel noise filtering of 3 gradient echoes acquired as 3-D multi-volume fMRI data
2. voxel-by-voxel estimation of T2* at all acquired repetition times

These 2 steps are ***not independent***: Step 2, the T2* estimation, can not be done before the input data have been processed by Step 1, the temporal voxel-by-voxel noise filtering.

The ***input data*** must contain three .nii files named *Echo1*.nii, *Echo2*.nii and *Echo3*.nii files containing fMRI echo series, as well as three .mat files named *Echo1*.mat, *Echo2*.mat and *Echo3*.mat containing DICOM information related to *Echo1*.nii, *Echo2*.nii and *Echo3*.nii.

Location of the datasets: the datasets used so far are placed on the CBIA ***gryf*** data server in the directory /data/common/PROJECTS/_Current/CEITEC_T2star/T2star_data.

An ***example dataset*** that can be immediately used by the CBIA as input to temporal voxel-by-voxel noise filtering is located at /data/common/PROJECTS/_Current/CEITEC_T2star/T2star_data/Example

Installation of the tool: simply place the T2star_github directory to a location of your choice.

Startup of the tool:

- launch MATLAB >=2016b
- change to your T2star_github directory

The tool was developed and tested using *MATLAB 2016b* under *Windows 7* and *WIndows 10*.

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1. Voxel-by-voxel noise filtering of the time-course of 3 fMRI gradient echoes.

This part of the tool is described in a paper to appear in ...

1.1 the noise problem

...

1.2 The denoising algorithm.

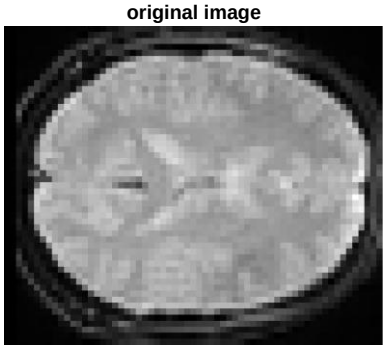
...

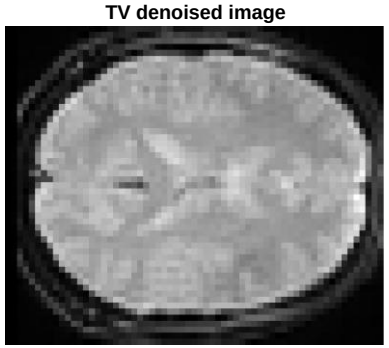
1.3 Running the MATLAB implementation of the denoising algorithm.

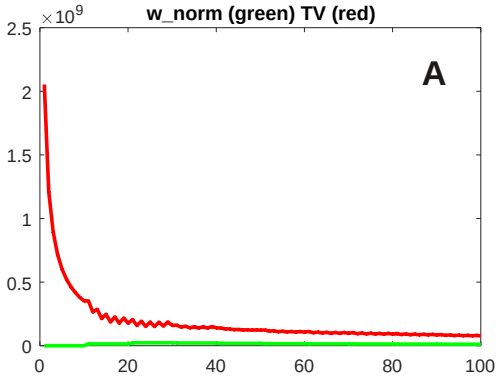
...

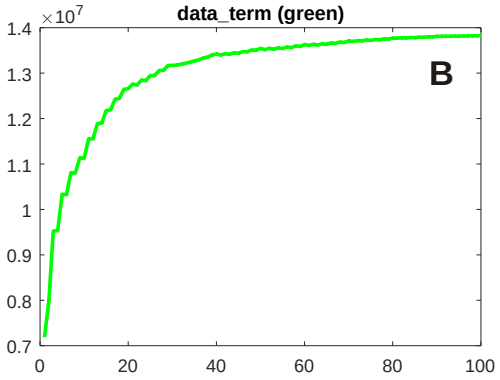
The denoising algorithm is encapsulated in the script named T2star_TV_T2star github.m which calls several other scripts and one mex-function.

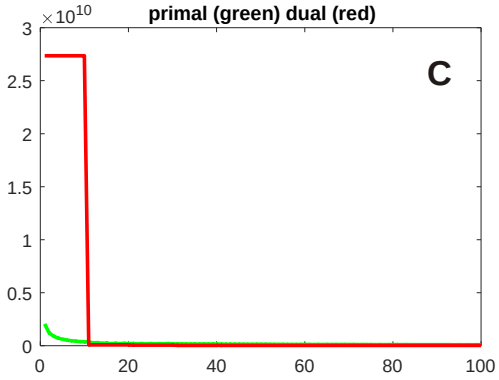
On completion of each echo's denoising, the algorithm creates a summary plot which helps pinpoint parameters that should be adjusted to obtain optimum convergence, as explained further on:











The denoising script is launched by the command

```
>> T2star_TV_github
```

after which a self-explanatory dialog follows.

Algorithm notifications are usually introduced by “CBIA>>” to distinguish them from system messages.

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```
CBIA>>please make sure spm12 toolbox is on your MATLAB path
```
Prompts for user actions are mostly terminated by a colon:
```
CBIA>>please enter full directory path containing
      xxx_Echo_N.nii and
      yyy_Echo_N_dicom_header.mat,
      such as I:\Data\T2star\4055B\FCNI1_mag\cwu:
```
while informative messages about the algorithm progress begin with an ellipsis (...):
```
CBIA>>...unfiltered echoes will be read from
         I:\Data\T2star\4055B\FCNI1_mag\cwu
CBIA>>...reading 4-D echoes Echo_1, Echo_2, Echo_3
         and Echo_1_dicom_header, Echo_2_dicom_header, Echo_3_dicom_header
CBIA>>...reading TE(1),TE(2),TE(3) and TR from dicom headers
CBIA>>...concatenating 4-D echoes Echo_1, Echo_2, Echo_3
         to 5-D datacube Echoes with echo number as the 5-th dimension
-------------------------------------------------------------------
```
Denoising is performed on 3-D volumes of all 3 echo trains for all fMRI-acquired time instants.

A z-slice is selected here for 2-D visual representation only, and does not affect denoising:
```
CBIA>>pick a z-slice, or press RETURN for default: [23]:
-------------------------------------------------------------------
```
To speed up computations by parallel processing on multi-core CPUs, the number of threads of the user's CPU can be entered:
```
CBIA>>enter number of CPU threads, or press RETURN for 8 threads:
-------------------------------------------------------------------
```

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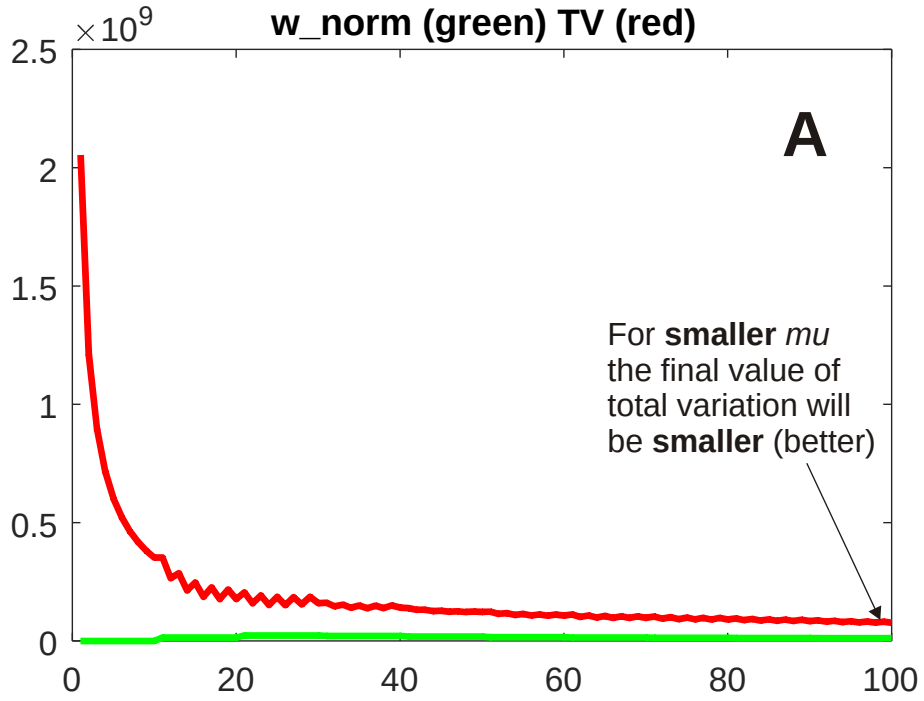
Setting the algorithm parameters:

```
CBIA>>enter log2(mu), or press RETURN for default [-16]:
```

The parameter `mu=2^log2(mu)` defines weighting of the L2-norm (mean square error) between the measured and the denoised echo time-course: the smaller `mu`, the smoother, in terms of total variation **TV**, will the denoised signal be. `mu` affects the speed and the stability of the TV optimization process.



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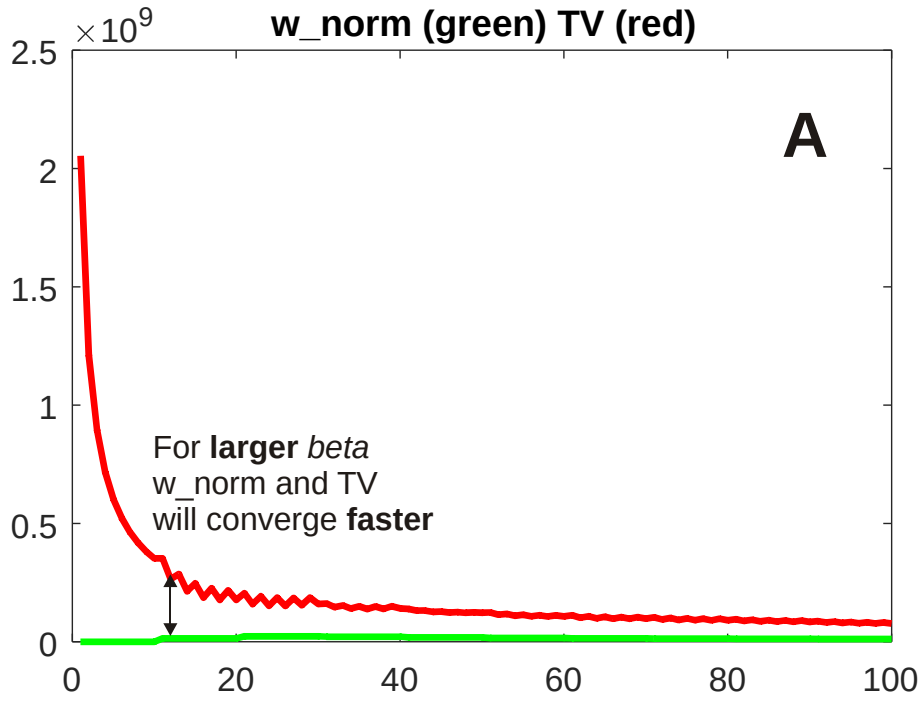
`CBIA>>enter log2(beta), or press RETURN for default [-6]:`

The parameter `beta=2^log2(beta)` affects the speed with which the true total variation TV will approach its approximation w_norm: the larger `beta`, the faster will **TV** and **w_norm** meet. `beta` affects the speed and the stability of the TV optimization process.



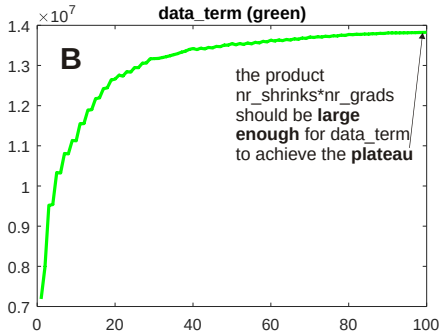
`CBIA>>enter nr_shrinks, or press RETURN for default [10]:`

The parameter `nr_shrinks` defines the number of **shrinkage** iterations, i.e.those in which total variation TV is reduced. `nr_shrinks` affects the accuracy of the TV optimization process.

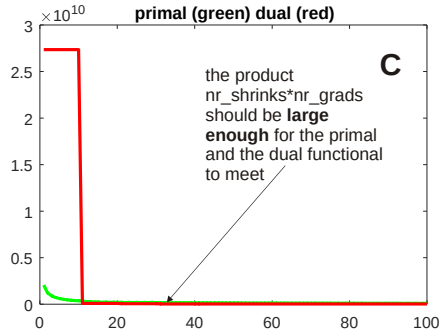
`CBIA>>enter nr_grads, or press RETURN for default [10]:`

The parameter `nr_grads` defines the number of **steepest descent** operations, i.e.those in which square error data_term between the filtered and the noisy echo is reduced. `nr_grads` affects the accuracy and the stability of the data_term optimization process.

The product `nr_shrinks*nr_grads` should be large enough for the *data_term* to reach the plateau:



Also, the product `nr_shrinks*nr_grads` should be large enough for the **primal** and the **dual** functional **to meet:**



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```
-----------------------------------------------------------------------
CBIA>>...TV filtering results will be stored in
         I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10
-----------------------------------------------------------------------
```

The algorithm progress is reported:

```
CBIA>>...temporal TV filtering of Echo_1
shrink_count=1
shrink_count=2
shrink_count=3
shrink_count=4
shrink_count=5
shrink_count=6
shrink_count=7
shrink_count=8
shrink_count=9
shrink_count=10
ElapsedTime= 176.0191
CBIA>>...temporal TV filtering of Echo_2
shrink_count=1
shrink_count=2
shrink_count=3
shrink_count=4
shrink_count=5
shrink_count=6
shrink_count=7
shrink_count=8
shrink_count=9
shrink_count=10
ElapsedTime= 176.7533
CBIA>>...temporal TV filtering of Echo_3
```

```
shrink_count=1
shrink_count=2
shrink_count=3
shrink_count=4
shrink_count=5
shrink_count=6
shrink_count=7
shrink_count=8
shrink_count=9
shrink_count=10
ElapsedTime= 178.1268
CBIA>>...saving TV filtering results to
         I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10
-----------------------------------------------------------------
```

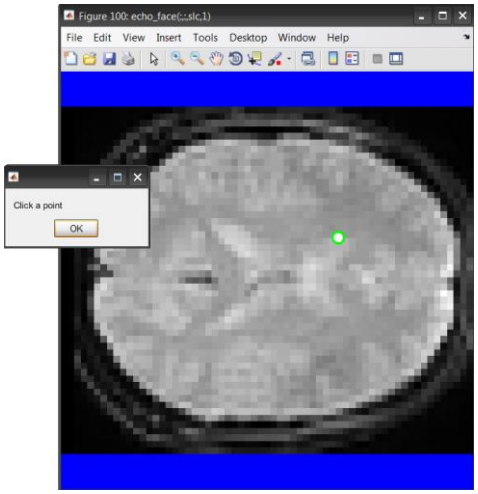
after which the termination notification appears:

```
CBIA>>...temporal TV filtering of the 5D datacube has been completed.
```

```
------------------------------------------------------------------------
```

Finally the user is prompted to peruse the denoising results:

```
        To visually compare unfiltered and TV-filtered echoes at voxels of your choice,
        pick repeatedly those you are interested in.
```




```
pick_another_pixel:[return/0]
pick_another_pixel:[return/0] 0
>>
>>
```

2. voxel-by-voxel estimation of T2* at all acquired repetition times.

2.1 Estimation of T2 by weighted exponential matching of the three TV-filtered gradient echoes.*

The MATLAB tool is based on the original implementation of the algorithm described in *Michálek et al.*:"Fast and accurate compensation of signal offset for T2 mapping", https://link.springer.com/article/10.1007/s10334-019-00737-3, which processed only single 2D slices of the input MRI data. For use with 3D fMRI data, the original code has been enhanced to include also the *z*-dimension (volume) and *t*-dimension (time). Resulting T2* estimates and noise masks are output as 4-D .nii files.

*2.2 Running the T2*estimation MATLAB script.*

The T2*estimation script is launched by the command

```
>> T2star_series_WLS_MFL
```

after which a self-explanatory dialog consisting of informative messages (introduced with ...) or prompts for user action (terminated with:) follows:

```
CBIA>>...please make sure spm12 toolbox is on your MATLAB path
CBIA>>please enter full directory path containing TV-filtered echoes
      TV_Echo_1.nii, TV_Echo_2.nii and TV_Echo_3.nii
      such as I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10:
CBIA>>...TV-filtered echoes will be read from
         I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10
CBIA>>...reading 4-D TV-filtered echoes TV_Echo_1, TV_Echo_2, TV_Echo_3
CBIA>>...concatenating 4-D TV-filtered echoes TV_Echo_1, TV_Echo_2, TV_Echo_3
         to 5-D datacube Echoes with echo number as the 5-th dimension
CBIA>>...unfiltered echoes will be read from
         I:\Data\T2star\4055B\FCNI1_mag\cwu
CBIA>>...reading 4-D unfiltered echoes Echo_1, Echo_2, Echo_3
         and Echo_1_dicom_header, Echo_2_dicom_header, Echo_3_dicom_header
CBIA>>...concatenating 4-D unfiltered echoes Echo_1, Echo_2, Echo_3
         to 5-D datacube Ref_echoes with echo number as the 5-th dimension
CBIA>>...reading TE(1),TE(2),TE(3) and TR from dicom headers
CBIA>>maximum slice:46
```

```
-----------------------------------------------------------------------
```

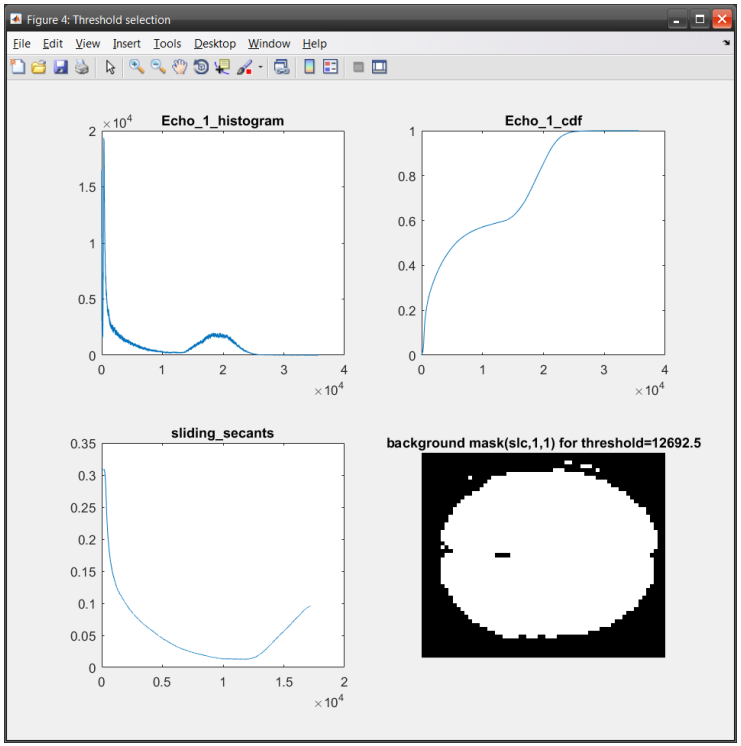
T2* estimation is performed on whole 3-D volumes for all fMRI acquired time instants.

z-slice is selected here for 2-D visual representation only, and does not affect denoising:

```
CBIA>>pick a z-slice for 2D visualizations, or press RETURN for default: [23]:
slc=23
-----------------------------------------------------------------------
```

Before starting the T2* estimation, a gray-value ***threshold*** separating background pixels from valid fMRI information is generated automatically. The threshold generation relies on the assumption that the histogram of Echo_1 array (i.e. the brightest echo) exhibits two distinct peaks. The user is presented a plot with the histograms as well as the threshold-generated background mask, and is given the possibility to change the threshold:

```
CBIA>>press RETURN to accept the threshold, or enter a different one: [12692.5]:
```



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```
-------------------------------------------------------------------
CBIA>>...interleaving 4-D TV-filtered echoes TV_Echo_1, TV_Echo_2, TV_Echo_3
         according to their absolute acquisition time
         to 4-D datacube interleaved_echoes
-------------------------------------------------------------------
CBIA>>...calculating T2star values for all volumes of input data
-------------------------------------------------------------------
```

The total execution time needed to estimate T2* for all voxels at all measured fMRI volumes is reported

```
ElapsedTime=34.8382
-------------------------------------------------------------------
```

and the directory where the 4-D results are saved as nifti files is displayed:

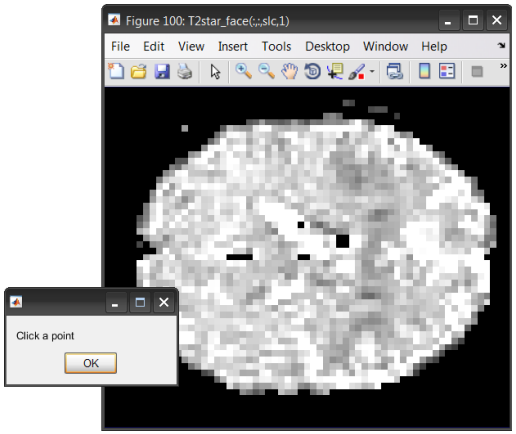
```
CBIA>>...saving noise mask and unmasked/masked T2star values as 4-D .nii files to
         I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10\T2star_series_WLS_MFL
-------------------------------------------------------------------
```

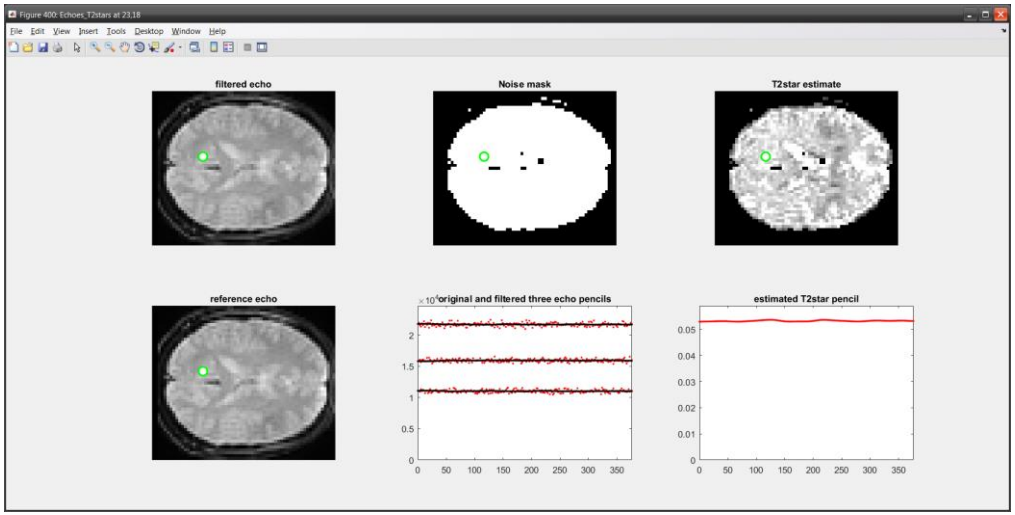
For the user-selected slice, some raw/limited/masked 3-D T2* maps and a noise mask are generated, visualized and saved as multipage tiffs in a slice-related directory. These can later be viewed, e.g., using *ImageJ*:

```
CBIA>>...extracting 3-D data at your selected slice number 23 for visualization
masked_pixel_ratio = 0.41266
CBIA>>...saving raw/limited/masked 3-D T2stars and noise mask at your selected slice number in
I:\Data\T2star\4055B\FCNI1_mag\cwu\TV_filtered_echoes\-16   -6   10   10\T2star_series_WLS_MFL\slc23
-------------------------------------------------------------------
```

And finally the user is given the possibility to to inspect the T2* time courses at voxels of their choice:

```
CBIA>>...To visually inspect echo and T2star time courses at voxels of your choice,
         pick repeatedly those you are interested in.
```






```
pick_another_pixel:[press RETURN for YES/0 for NO]
pick_another_pixel:[press RETURN for YES/0 for NO]
pick_another_pixel:[press RETURN for YES/0 for NO] 0
```

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