Visualizing very small density differences in pharmaceutical samples by using the Modified Bronnikov Algorithm

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Micro-CT (µCT) is a very useful tool in pharmaceutical sciences. It is able to visualize porosity in the whole sample without destroying it, making the risk of false results due to the sample treatment minimal. For this reason, this powerful technique is often used for pore analysis [1]. Apart from the pores, density distributions in pharmaceutical samples are also of interest. This information can give new insights in the behaviour of the sample.
However, these density differences are often very small, and hardly visible in noisy CT data. This problem can be solved by using the phase signal instead of the X-ray absorption. This phase signal is present in light objects such as most pharmaceutical samples and is more sensitive to density variations than the absorption. This makes it ideal for the visualization of these structures.

In pure phase objects, i.e. samples that have no absorption, the phase signal can be reconstructed using the Bronnikov filter[2]. In reality, all objects have a certain absorption coefficient, making the algorithm incorrect. However, by adding a correction parameter in the filter, an approximation of the phase signal can be retrieved. This method is called the Modified Bronnikov Algorithm (MBA)[3] and can be used for a wide variety of objects[4].

One of the main advantages of this algorithm is the removal of phase artefacts. As phase shift causes refraction, a typical black-white profile is seen in the X-ray projections. When these images are reconstructed with standard filtered back-projection, this intensity profile is also visible in the reconstructed slices as a very dense layer of the sample or feature, and a too low (or even negative) density just outside the feature. These densities are not physical thus unwanted in tomographic reconstructions. They also obstruct segmentation, making filtered data more suitable for porosity measurements, as can be seen in Fig. 1.

Besides this improved segmentation, analysis of a pharmaceutical sample showed new structures, not seen in standard filtered backprojection (Fig. 2). The sample is an extrusion of a polymer with a standard drug. After extrusion, a porous pill is obtained, where the drug crystals sustain the polymer matrix with the large pores. When the drug is dissolved in water, the polymer matrix collapses due to a lack of structural strength and the elasticity of the material. This reduced porosity can be seen and measured with microCT. When MBA is applied, denser pores become visible, indicating a change in polymer structure and density at the positions of the pores.

SEM analysis of the same sample showed spots without micropores, resulting in a higher density, and possibly a structural change. Two images of these collapsed pores can be seen on Fig. 3.

References

[1] D. Traini et al., *Microscopy and Microanalysis* 111 (2008) 13-15

[2] A.V. Bronnikov, *Opt. Comm.* 171 (1999) 239-244
[3] A. Groso et al., *Opt. Express* 14(18) (2006) 8103-8110
[4] M. Boone et al., *Nucl. Instr. Meth. Phys. Res. B.* accepted for publication

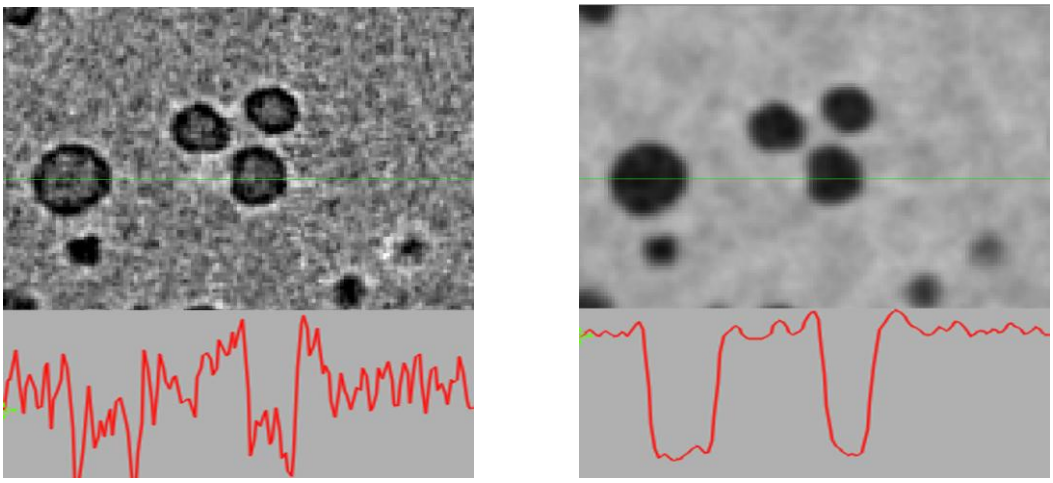

FIG. 1. Line profile on a standard filtered backprojection (left) and a MBA reconstructed slice (right).

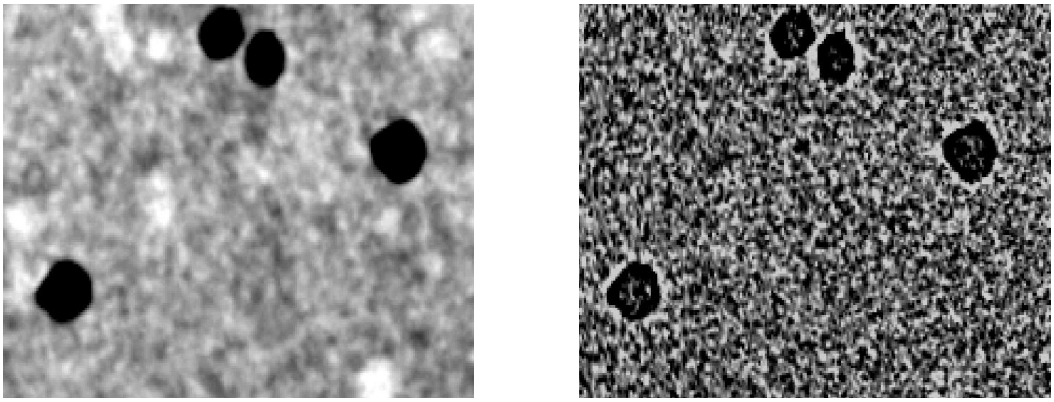

FIG. 2. FBP reconstructed image showing only pores (left) and MBA reconstructed slice showing both pores and dense regions (right).

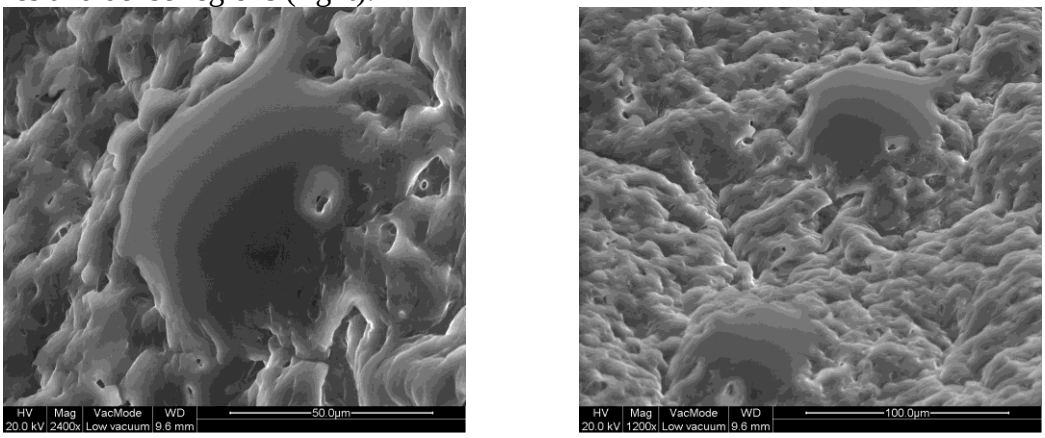

FIG. 1. Two views on the dense regions present in the sample after dissolution of the drug.