Real-time MRI of tablet disintegration: Visualization and Quantification

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Target Audience: Physicists or pharmacists who are interested in the visualization and quantification of disintegration processes.

Purpose: The efficiency of orally administered pharmaceutical dosage forms depends on the disintegration characteristics of the tablet. The most important parameter that is used to characterize the disintegration process of tablets is the disintegration time[1]. For research purposes, CCD cameras sometimes are used to visualize the disintegration process[2]. CCD cameras provide a high spatiotemporal resolution but they are limited to visualize surface changes during the tablet disintegration. Therefore, the main goal of this work was to introduce an MRI-based method that is able to visualize the interior of disintegrating tablets and to determine the disintegration time.

Methods: T1-weighted data sets were obtained using a spoiled radial FLASH sequence (TR/TE = 3/1.8 ms, flip angle = 5°, FOV = 25.6 × 25.6 mm^2, spatial resolution 0.080 × 0.080 × 0.600 mm^3) at 9.4 T (Bruker BioSpin, Germany). Signal detection was performed by a 4-channel rat coil array (Bruker BioSpin, Germany). 125 radial spokes (5 interleaved turns) together with a nonlinear inverse reconstruction[3] allowed for an acquisition time per image of 75 ms. Dynamic MRI data sets were acquired over a period of 28 seconds to cover the whole disintegration process. The acquisition starts one second before releasing the tablet into a water filled cavity. To increase the signal intensity the cavity was filled with distilled water doped with 2 mM of $CuSO_4$.

Tablets with 2% (n=6) or 16% (n=6) of a chosen disintegrant (Polacrilin Potassium) were used to visualize the disintegration process. The acquired data were normalized and corrected for surface coil signal inhomogeneity after reconstruction. A region of interest (ROI) including the whole cavity (doped water and tablet) was chosen to quantify the disintegration process. The ROI was quantified frame wise by calculating a histogram of the signal intensity.

Results: Time series of the disintegration process for a tablet containing 16% of the disintegrant are shown in Figure 1. The images were cropped for better illustration. During the first seconds the tablet began to swell in vertical direction. The disintegration process is visible during the selected frames shown in Figure 1. Figure 2 shows the frame wise histogram of the signal intensity for a single tablet containing 2% (right) and 16% (left) of the chosen disintegrant. The histogram was divided into three major sections ("tablet band", "transition zone" and "water band") as shown in Figure 2. The disintegration time corresponds to the temporal evolution of the "tablet band" and was defined as that point in time after which the width of the "tablet band" remained constant. The determined disintegration time was 1.76 ± 0.33 s for tablets containing 16 % and 3.01 ± 0.34 s for tablets containing 2% of the disintegrant.

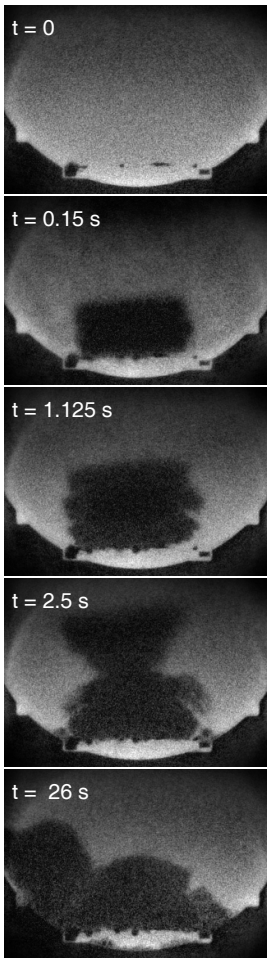

Fig. 1

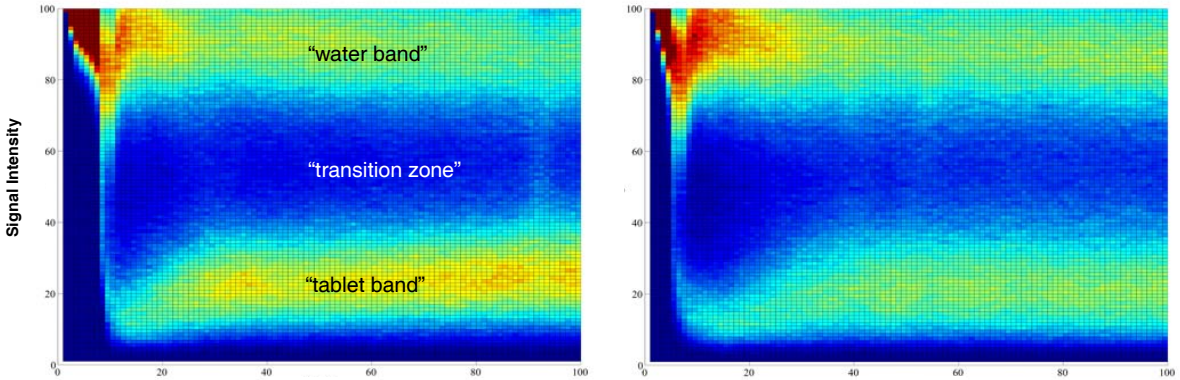

Fig. 2

Discussion: In contrast to conventional approaches that only observe the surface of tablets during the disintegration process via CCD cameras, the real-time MRI-based method proposed in this work is able to visualize the interior of disintegrating tablets. Moreover, the achieved spatiotemporal resolution with real-time MRI is sufficient to get a more detailed representation of the disintegration dynamics. The histogram analysis enables separate assessment of "tablet band", "water band" and "transition zone".

Conclusion: The introduced approach is capable to visualize the disintegration process and to determine the disintegration time of tablets. Moreover, the proposed histogram possesses information about mechanisms of the disintegration process that will be extracted and quantified in future works. In addition, the proposed real-time method may be able to visualize and quantify other disintegration or dissolving processes in material sciences.

References: **1.** European Pharmacopoeia 7.5, 2012 **2.** Mesnier X et al. A novel method to quantify tablet disintegration. Powder Technol 2012;doi:10.1016/j.powtec.2012.06.038 **3.** Uecker M et al.. Image reconstruction by regularized nonlinear inversion - Joint estimation of coil sensitivities and image content. Magn Reson Med 2008;60:674-682.