In-situ Monitoring of Powder Density Using Terahertz Pulsed Imaging

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***Abstract*—We have developed an approach to investigate density variations in a moving powder bed by means of terahertz pulsed imaging. Terahertz measurements were acquired continuously during the rotation of a container filled with different grades of lactose and microcrystalline cellulose powder. Relative density distributions were resolved for different compaction stages of the powder, which indicated high variations of the powder density.**

I. INTRODUCTION

Granular materials, namely a large conglomeration of macroscopic particles, play an important role in many industries, such as mining, agriculture, construction, food and pharmaceuticals. Almost every consumer product and medication originate from a formulation in granular form. Although a granular material might look simple, it behaves differently to solids, liquids or gases. The densification of a granular material is particularly complex, but at the same time its understanding is crucial, especially in manufacturing solid oral dosage forms. It is therefore of great importance for the pharmaceutical industry to measure relative density in a non-destructive and contactless manner during production.

A very promising method to measure the relative density of pharmaceutical materials is terahertz technology as it has been demonstrated for powder compacts (pharmaceutical tablets) of various formulations [1]. The relative density of tablets is typically calculated from the effective refractive index of the compact measured by terahertz time-domain spectroscopy [1]. Since terahertz radiation can relatively easily penetrate through typical pharmaceutical materials, most previous studies focused on measuring samples in transmission which was demonstrated for tablet thicknesses of up to 5.3 mm [2]. However, transmission measurements are not always feasible in an industrial setting and hence the use of a reflection configuration is often the preferred option. This is also the case for monitoring powder density in pharmaceutical capsule filling processes, where the relative density of the powder directly impacts the weight in a capsule. Since the weight of the powder in a capsule is directly related to its drug content, the relative density of the powder in the container - where the capsule is filled from – is considered as a critical performance-related property [3]. The aim of this study was to quantify and spatially resolve density variations in a rotating container filled with powder by means of terahertz reflection technology.

II. MATERIALS AND METHODS

The experimental setup (Fig. 1) resembles a pharmaceutical capsule filling process. We investigated three grades (varying true density and particle size) of two different materials, i.e. lactose (Lactohale 100, 200 and 220) and silicified microcrystalline cellulose (sMCC 50, sMCC 50LD and sMCC 90). These six powders specifically differ in their compressibility behaviours, which facilitates the investigation of the sensitivity and applicability of the method. We adjusted the pressure on the powder bed by tightening a nut on the central screw that was used to assemble the compression unit and the powder container. Three load sensors connected to a computer via an Arduino Uno were used to measure the applied force prior to each compaction stage. The average nominal relative density, $\bar{\varrho}_r = m/A\bar{h}\varrho_t$, of the powder was calculated by using the known cross-section area of the container, A, and true density, ϱ_t, of the respective powder as well as measuring the powder bed height, h, at eight different position uniformly distributed around the container (Fig. 1b). An average value of the powder bed height, $\bar{h}$, was then used to calculate $\bar{\varrho}_r$. The container was rotated at a speed of 4 rpm for all experiments.

We used a commercial time-domain terahertz spectrometer (TeraPulse 4000, TeraView Ltd, Cambridge, UK) coupled with a fibre-based flexible reflection probe. The system was

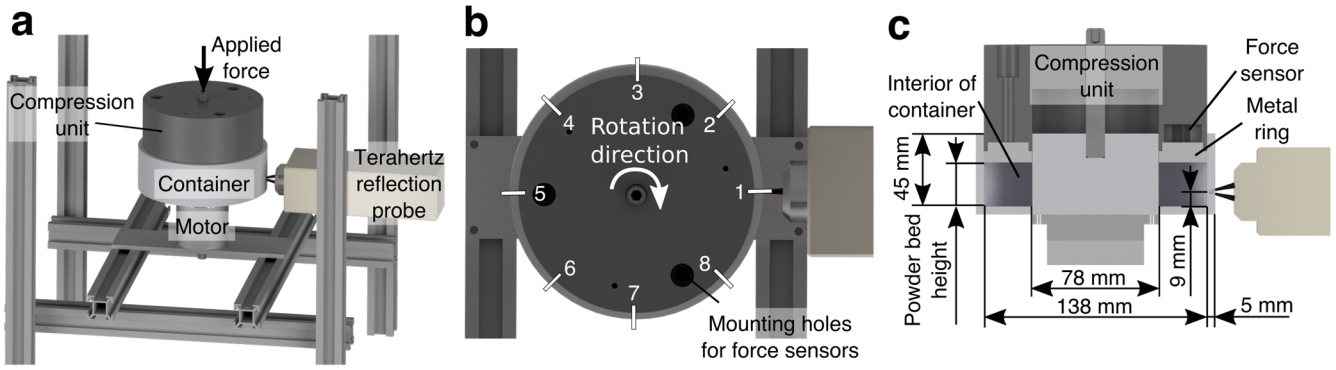

Fig. 1. Experimental setup for the *in-situ* monitoring of the relative density at the powder/container interface. (a) A motor rotated the container which was filled with the powder. The compression unit was equipped with three force sensors to determine the applied pressure on the power. (b) Top view of the setup indicating the eight measurement positions of the powder bed height, i.e. compression displacement. (c) Cross-section view of the setup depicting the dimensions of the container, the measurement position as well as the position of the force sensors.

configured to acquire the reflected terahertz pulse over an optical time delay of 45 ps and at an acquisition rate of 15 Hz. The reflection probe was equipped with a silicon lens with a focal length of 18 mm. We continuously acquired 2000 waveforms at each compression step while the container was rotating, which yielded a total measurement time of 133 s. A narrow strip of copper foil was fixed onto the outside of the container, which reflected the terahertz pulse and served as a datum to facilitate the automatic detection of a full rotation from the terahertz waveforms. Seven full rotations were averaged which yielded $N = 230$ terahertz waveforms uniformly distributed around the container circumference.

We assumed that the terahertz beam is focused at normal incidence on the high-density polyethylene (HDPE) container, and that absorption of the HDPE container and the reflection from the air/container interface are negligible in order to simplify the calculation of the surface refractive index, n_p, from the reflection measurements. Although these assumptions introduce a minor systematic error on the absolute magnitude of the calculated n_p, they do not affect the prediction of the relative density from the terahertz measurements. Based on the definition of the Fresnel reflection coefficient, r_{cp}, we could determine $n_p = n_c(r_{cp} + 1)/(n_c(r_{cp} + 1))$ with $n_c = 1.54$ [4], where subscript c denotes container and p for the powder bed. r_{cp} was calculated by relating the amplitude of the reflected pulse from the container/powder interface to a reflection from the copper foil on the container.

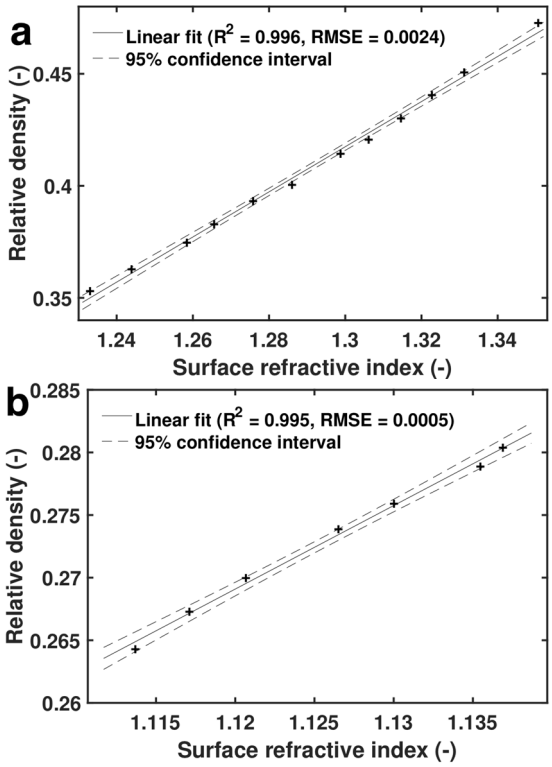

Fig. 1. The relative density, $\bar{\varrho}_r$, as a function of the surface refractive index, $\bar{n}_p$, calculated from the terahertz measurements for (a) Lactohale 220 and (b) sMCC 50LD.

III. Results

Terahertz reflection measurements were acquired continuously during the rotation of the container. Since the container material (HDPE) was transparent to terahertz radiation, the reflection from the container/powder interface could be readily observed in the terahertz time-domain waveform. An increase in relative density of the powder caused a reduction of the reflection amplitude from the container/powder interface. A reduction of the amplitude is related to an increase in the surface refractive index, n_p, of the powder. n_p was thus calculated from the terahertz reflection measurements and we reveal in this study that the surface refractive index averaged around the entire container, $\bar{n}_p$, is linearly related to $\bar{\varrho}_r$ for the six different investigated powders. These observations are in line with our previous studies about the relative density of powder compacts, where the refractive index is also linearly related to the porosity [1]. A linear model was thus fitted for each material to relate $\bar{n}_p$ to

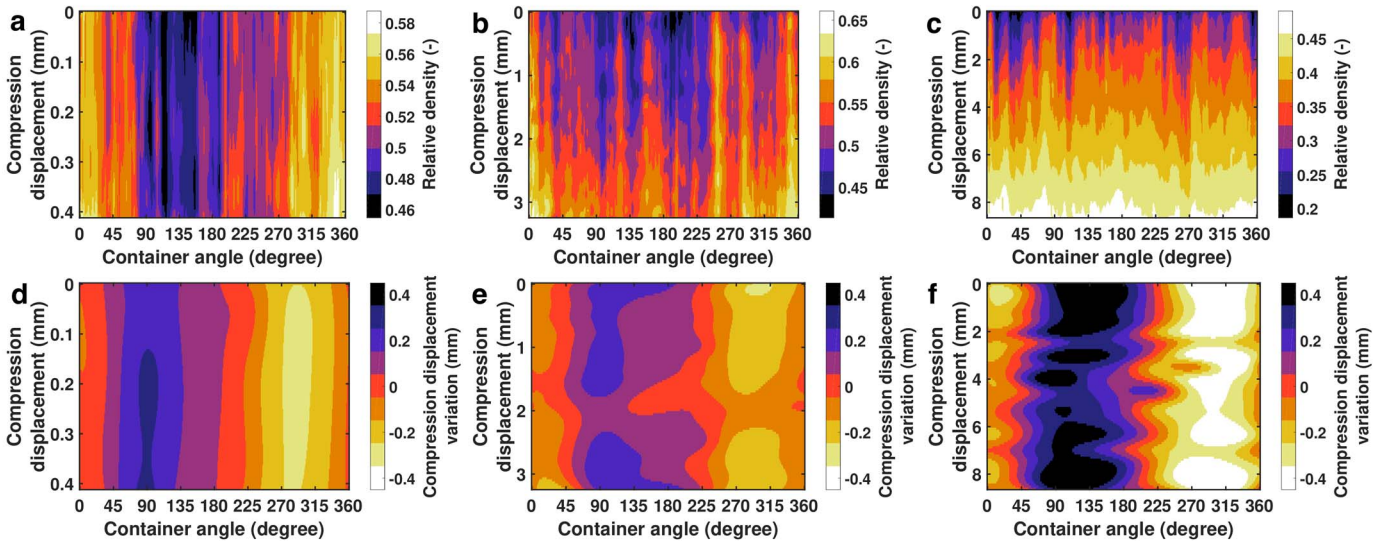

Fig. 2. Maps of relative density distributions (a-c) and powder bed height variations (d-e) as a function of the angle on the container. (a,d) Lactohale 100, (b,e) Lactohale 200, (c,f) Lactohale 220. The data was interpolated using a cubic interpolation. The compression displacement represents the change of powder bed height from its initial height.

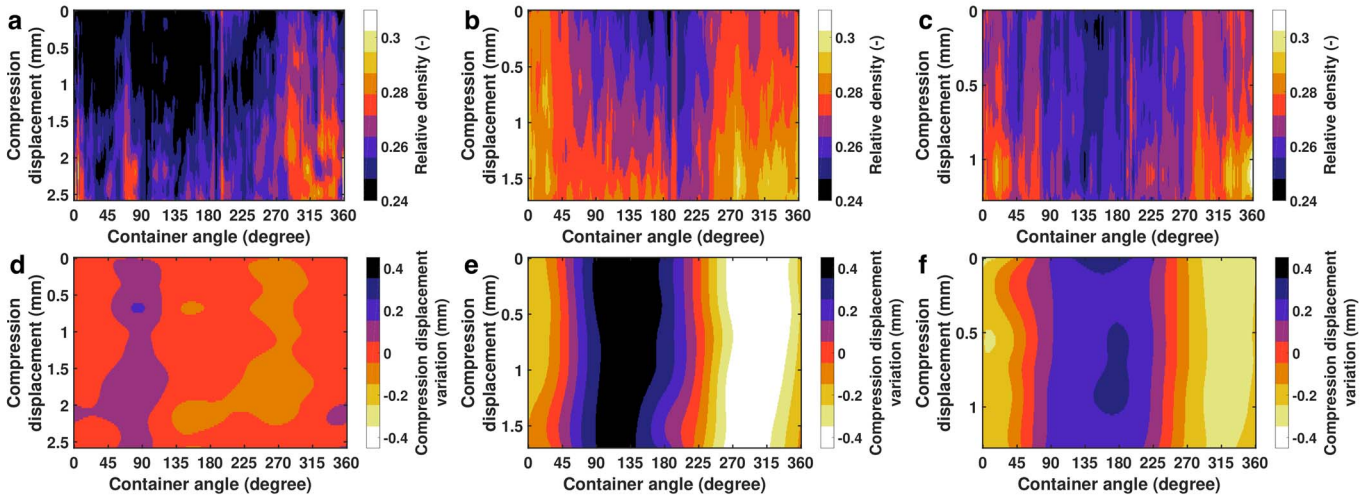

Fig. 3. Maps of relative density distributions (a-c) and powder bed height variations (d-e) as a function of the angle on the container. (a,d) MCC 50, (b,e) MCC 50LD, (c,f) MCC 90. The data was interpolated using a cubic interpolation. The compression displacement represents the change of powder bed height from its initial height.

$\bar{\varrho}_r$ in order to predict the powder density from each individual terahertz reflection measurements (Fig. 2 and 3). The results indicate non-uniform relative density distributions across the powder bed, which would result in a high variation of drug content between different capsules.

The measurement of the powder bed height at eight different positions of the container facilitates the investigation of density variations and powder bed height variations at a specific angle of rotation.

We clearly observe a relationship between the local density variations (Fig. 2a and b) and the measured powder bed height variations (Fig. 2d and e) as a function of the container angle for Lactohale 100 and 200. Moreover, these data of Lactohale 100 reveal that applying normal stress to the powder does not impact the uniformity of the powder bed, as reflected by the horizontal color distribution along vertical direction. We also observed local density variations for Lactohale 200 indicating a non-uniform distribution of the powder density upon compaction (Fig. 2b and e). Therefore, density variations around the container are introduced before applying pressure on the powder and they remain in the powder bed throughout the compaction process. This is primarily attributed to the filling process which introduces initial variation in the powder bed height that yield a non-uniform relative density distribution. In contrast, Lactohale 220 exhibits different stages of powder bed variations throughout compaction. At low compression displacements relative density variations in the horizontal direction were detected, which increase upon compaction but again decrease at smallest powder bed height (Fig 2c and f).

The sMCC materials undergo a smaller change in relative density variations (Fig. 3). Predicted relative density variations are reflected by variations in powder bed height variations for all sMCC materials. Surprisingly, we observe similarities of SMCC 50 LD (Fig. 3b) and SMCC 90 (Fig. 3c), which have very different material attributes, for example the particle size. Since the particle size amongst other factors such as particle shape, elasticity/plasticity/brittleness is known to affect the strength of interparticulate bonds and arrangements of particles in a powder bed, we would have expected similar distribution maps between SMCC 50 (Fig. 3a) and SMCC 50 LD (Fig. 3b). However, the two powders clearly differ in their bulk densities (sMCC 50: 0.31 g cm^{-3}, sMCC 50LD: 0.24 g cm^{-3}), where sMCC 50LD has a lower bulk density as also evident from the sample label "LD" (low density). sMCC 90 on the other hand has a similar bulk density as sMCC 50. It is well known, that a lower density may facilitate compressibility, i.e. the densification of a powder bed due to the application of a stress. The observed local areas with higher relative density of sMCC 50LD (see Fig. 3b) are attributed to differences in bulk density rather than the particle size. These findings are also reflected in the resulting maps of powder bed height variations (Fig. 3d-f), which again indicate and support the presence of local density variations within the powder bed.

IV. Summary

We demonstrated the analysis of powder density variations in a rotating container by means of terahertz reflection measurements. The ability to spatially resolve density variations within a powder bed is of interest for wide range of industrial applications/processes/unit operations; especially for processes where density variations of the bulk powder can result in out-of-spec end products. The proposed method has also great potential to quantitatively measure bulk density variations of a static or moving powder bulk/powder stream.

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