Terahertz Frequency Domain Sensing for Fast Porosity Measurement of Pharmaceutical Tablets

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ABSTRACT

Porosity is an important property of pharmaceutical tablets since it may affect tablet disintegration, dissolution, and bio-availability. It is, therefore, essential to establish non-destructive, fast, and compact techniques to assess porosity, in-situ, during the manufacturing process. In this paper, the terahertz frequency-domain (THz-FD) technique was explored as a fast, non-destructive, and sensitive technique for porosity measurement of pharmaceutical tablets. We studied a sample set of 69 tablets with different design factors, such as particle size of the active pharmaceutical ingredient (API), Ibuprofen, particle size of the filler, Mannitol, API concentration, and compaction force. The signal transmitted through each tablet was measured across the frequency range 500-750 GHz using a vector network analyzer combined with a quasi-optical set-up consisting of four off-axis parabolic mirrors to guide and focus the beam. We first extracted the effective refractive index of each tablet from the measured complex transmission coefficients and then translated it to porosity, using an empirical linear relation between effective refractive index and tablet density. The results show that the THz-FD technique was highly sensitive to the variations of the design factors, showing that filler particle size and compaction force had a significant impact on the effective refractive index of the tablets and, consequently, porosity. Moreover, the fragmentation behaviour of particles was observed by THz porosity measurements and was verified with scanning electron microscopy of the cross-section of tablets. In conclusion, the THz-FD technique, based on electronic solutions, allows for fast, sensitive, and non-destructive porosity measurement that opens for compact instrument systems capable of in-situ sensing in tablet manufacturing.

1. Introduction

In the pharmaceutical industry, tablets are one of the most convenient dosage forms for the administration of drugs to patients. Pharmaceutical tablets consist of one or more active pharmaceutical ingredients (API) and excipients. The physical and chemical properties of both API and excipients affect the tabletting process and the physical properties of tablets. Porosity, which is the ratio between the air void volume and total bulk volume, is one of them and may play a crucial role in the disintegration and dissolution time of tablets (Ervasti et al., 2012). Recently, the pharmaceutical industry has been moving toward continuous manufacturing, and there is a high need for fast and non-destructive techniques to monitor the porosity of tablets during the production process. However, there is no in-line technique for monitoring of porosity during tablet manufacturing (Naftaly et al., 2019) and off-line techniques are typically destructive and slow.

Mercury porosimetry (Westermarck et al., 1998) and Thermoporometry (Luukkonen et al., 2001) are common reliable methods for porosity measurements with the disadvantage of being destructive. X-ray computed micromotography (Markl et al., 2017) and helium pycnometry (Sereno et al., 2007) are reported as non-destructive techniques. X-ray computed micromotography is advantageous for pore structure analysis. Helium pycnometry provides information about average porosity. However, these techniques are slow and not suitable for in-situ sensing, such as for at-line and in-line measurements in manufacturing processing operations. Gas in Scattering Media Absorption Spectroscopy (GASMAS) (Sjöholm et al., 2001; Svensson et al., 2007; Johansson et al., 2021) is a non-destructive and at-line technique to measure optical porosity. Dielectric characterisation of tablets using terahertz time-domain spectroscopy (THz-TDS) has recently emerged as a non-destructive tool for porosity measurements (Lu et al., 2020). Juuti et al. used a THz spectrometer to demonstrate the correlation between the effective refractive index and tablet porosity (Juuti et al., 2009). Bawuah et al. used THz-TDS to obtain the porosity of tablets composed of one excipient (MCC) (Bawuah et al., 2014) and later tablets consisting of several excipients and an API (Bawuah et al., 2016). Naftaly et al. proposed the use of THz-TDS coupled with an index-matching material as a destructive technique to analyse the open porosity and scattering loss of powder compacts (Naftaly et al., 2020). Skelbek-Pedersen et al. used THz-TDS to study particle fragmentation during tabletting and showed that initial particle size and deformation behaviour of the particles affect the correlation between effective refractive index and porosity (Skelbek-Pedersen et al., 2020). Recently, Stanzinger et al. demonstrated a lab-experimental set-up for monitoring powder flow densification, which is inversely proportional to porosity, with THz-TDS (Stranzinger et al., 2019). Whilst THz-TDS instrumentation is a versatile tool for dielectric characterisation in a lab environment, it is difficult to miniaturise and implement as a stable, reliable,
In this work, we evaluated the THz frequency-domain (THz-FD) technique, to our knowledge for the first time, as a candidate for a future miniaturized in-line porosity measurement system. The miniaturization capabilities of electronic sources and receivers (Sengupta et al., 2018; Hillger et al., 2019), makes THz-FD promising for a future compact, fast, and non-destructive measurement system (Neumaier et al., 2014; Dahlbäck et al., 2012) for in-situ porosity measurements during pharmaceutical processing operations. In our previous work (Moradi et al., 2019), we showed that THz-FD is an effective technique for the characterization of pharmaceutical tablets with different dielectric constants. In this paper, we have explored the applicability of the THz-FD technique to porosity sensing by studying the effect of varying design factors in a tablet formulation on the effective refractive index and, consequently, porosity. The design factors were API and filler particle size, API concentration, and compaction force. The effective refractive index was directly extracted from the measurements of complex transmission coefficients across the frequency range 500-750 GHz. In order to transfer effective refractive index from THz measurements to porosity, an empirical linear relation between effective refractive index and tablet density was used. Moreover, fragmentation behaviour of API and filler particles was observed in THz measurement results and validated with scanning electron microscopy of the tablets.

2. Methodology

2.1. Tablet Preparation

In this work, we studied a sample set of 69 tablets consisting of Ibuprofen as an API, Mannitol as an excipient, and Magnesium stearate as a lubricant. A full factorial design of API particle size at two levels ($d_{50} \sim 71, 154 \mu m$) and excipient particle size at two levels ($d_{50} \sim 91, 450 \mu m$) was set up, where the $d_{50}$-value is the median diameter of the particle size distribution found at 50% in the cumulative distribution. This design was repeated at five API concentration levels ($\sim 16, 18, 20, 22, 24 \text{ w/w\%}$), and Magnesium stearate concentration was kept constant at $\sim 1 \text{ w/w\%}$ for all tablets. Details about the samples are provided in (Sparén et al., 2015) and a summary is given in the table 1, where experiments 21–23 are center points. Further information can be found in the table S1 in the supplementary. Tablets from all powder blends were manufactured at three compaction forces ($\sim 8, 12, 16 \text{ kN}$), resulting in 69 different tablet types. All tablets were flat-faced, with a nominal weight of 300 mg, a diameter of 10.0 mm, and a thickness, $l$, in the range of 2.9–3.4 mm measured using a digital micrometer. We used a scanning electron microscope (Zeiss Supra 55), with an accelerating voltage of 5 kV to optically inspect the cross section of one tablet (experiment number 3 in the table 1). The cross-section of the tablet was coated with a 20-nm film of sputtered aluminium under vacuum.

| Experiment number | API particle size $d_{50}$ ($\mu m$) | Filler particle size $d_{50}$ ($\mu m$) | API concentration (w/w%) |
|-------------------|-----------------------------------|-------------------------------------|--------------------------|
| 1                 | 71                                | 91                                  | 16                       |
| 2                 | 154                               | 91                                  | 16                       |
| 3                 | 71                                | 450                                 | 16                       |
| 4                 | 154                               | 450                                 | 16                       |
| 5                 | 71                                | 91                                  | 18                       |
| 6                 | 154                               | 91                                  | 18                       |
| 7                 | 71                                | 450                                 | 18                       |
| 8                 | 154                               | 450                                 | 18                       |
| 9                 | 71                                | 91                                  | 20                       |
| 10                | 154                               | 91                                  | 20                       |
| 11                | 71                                | 450                                 | 20                       |
| 12                | 154                               | 450                                 | 20                       |
| 13                | 71                                | 91                                  | 22                       |
| 14                | 154                               | 91                                  | 22                       |
| 15                | 71                                | 450                                 | 22                       |
| 16                | 154                               | 450                                 | 22                       |
| 17                | 71                                | 91                                  | 24                       |
| 18                | 154                               | 91                                  | 24                       |
| 19                | 71                                | 450                                 | 24                       |
| 20                | 154                               | 450                                 | 24                       |
| 21                | 95                                | 211                                 | 20                       |
| 22                | 95                                | 211                                 | 20                       |
| 23                | 95                                | 211                                 | 20                       |

Figure 1: a) Photograph and b) schematics of the experimental set-up showing THz S-parameter measurements in transmission mode. The blue square represents the area showed in the photograph.
2.2. Measurement set-up

To investigate the tablets, the effective refractive index was extracted from complex transmission coefficients, $S_{21}$, measured at 500-750 GHz and translated into porosity. The measurement set-up consisted of a vector network analyzer (Keysight PNA-X) with VDI frequency extenders WM380 and quasi-optical components, see Fig. 1a. The frequency range was selected to avoid scattering effects (long wavelength compared to the particle size), absorption peaks, and at the same time to ensure a small beam size compared to the tablets’ diameter. During measurements, the intermediate frequency bandwidth was set to 1 kHz. In order to visualize and help with the alignment of the quasi-optical set-up, the vector network analyzer was calibrated at the interface between the waveguide flanges of the extenders and the horn antennas using the SOLT (Short, Open, Load, Through) method. The signal was then focused on the tablets using four gold protected off-axis parabolic mirrors with a focal length of 76.4 mm, see Fig. 1b. The estimated beam diameter at the focal point is approximately 2 mm. Each of the 69 samples was measured ten times in consecutive frequency sweeps to verify the measurement repeatability and estimate the effect of additive white Gaussian noise. Before each tablet measurement, the empty sample holder was measured as a reference for relative measurements. Relative measurements suppressed uncertainty due to possible misalignment of components, loss in the optical path, and temperature and humidity variation. Each frequency sweep took less than one second to complete. The temperature and humidity were recorded during the measurements and varied in the ranges 22.6-22.9 °C and 21-30 %, respectively.

2.3. Effective Refractive Index Extraction

The effective complex refractive index of the samples, $\tilde{n}_s = n_s - jk_s$, can be extracted from a relative measurement of the complex transmission coefficient, $T = S_{21}$, between the sample and the empty holder (air), and its comparison to a model (Zhu and Wu, 2021).

The relative transmission between sample and air, $T_s/T_a$, can be modeled as in equation 1, which considers the multiple reflections inside the tablet (Nicolson and Ross, 1970).

$$\left( \frac{T_s}{T_a} \right)_m = \frac{(1 - \Gamma^2)}{1 - \Gamma^2 e^{-2jk_0l}} e^{-jk_0(\tilde{n}_s - 1)},$$

(1)

where $k_0$ is the free space wave number, $l$ is the thickness of the tablet and $\Gamma$ is the complex reflection coefficient, which in this case is:

$$\Gamma = \frac{1 - \tilde{n}_s}{1 + \tilde{n}_s}.$$  

(2)

Thick tablets, compared with the wavelength, result in multiple wavelengths inside tablets and therefore phase ambiguity (Bourreau et al., 2006). In order to address the phase ambiguity and extract $\tilde{n}_s$, the steps below were followed.

Step 1: A linear fit of the phase of measured relative transmission, $\phi = \text{Arg}(T_s/T_a)_m$, across frequency was used to find the average refractive index as an initial estimate for $n_s$, $n_{sj}$, using equation 3 (Weir, 1974):

$$n_{sj} = 1 + \frac{r c}{2 \pi f},$$

(3)

where $c$ is the speed of light in vacuum, and the time delay, $r = -\frac{\Delta \phi}{\Delta \phi}$, is the slope of the linear fit (Mrnka et al., 2022).

Step 2: The value of $\tilde{n}_s$ versus frequency was obtained numerically by solving equation 4:

$$f(\tilde{n}_s) = \left( \frac{T_s}{T_a} \right)_m - \left( \frac{T_s}{T_a} \right)_d = 0.$$  

(4)

This equation has multiple possible solutions because of the periodic nature of the exponential terms. To find the correct solution, the $n_{sj}$ value from step 1 was used as an initial estimate.

Step 3: Finally, the model, $(T_s/T_a)_m$, was recalculated using $\tilde{n}_s$ obtained in step 2, and its magnitude and phase were compared with the measurement data, $(T_s/T_a)_d$.

2.4. Tablet Porosity Calculation

We extracted THz porosity, $f_{THz}$, from the effective refractive index, $n_s$, obtained from the THz measurements. $f_{THz}$ can be obtained as in (Sun, 2004):

$$f_{THz} = 1 - \frac{\rho_{lab,THz}}{\rho_{true}},$$

(5)

where $\rho_{lab,THz}$ is the tablet density and $\rho_{true}$ is the true density, which is the density of the particles in the powder formulation. $\rho_{lab,THz}$ was obtained from the effective refractive index extracted from THz measurements by an empirical linear relation between tablet density and effective refractive index, as in (Moradi et al., 2019):

$$\rho_{lab,THz} = \rho_1 n_s + \rho_0.$$  

(6)

In order to obtain the coefficients, $\rho_0$ and $\rho_1$, for this specific set of tablets, the tablet density obtained from mechanically measured mass and volume of the samples was used for calibration.

$\rho_{true}$ in equation 5 was calculated from the concentration, $w_i$, and the true density of the ingredients, $\rho_{true,i}$, from literature (Nokhodchi et al., 2015) and their data sheet, as in (Sun, 2004):

$$\frac{1}{\rho_{true}} = \sum_{i=1}^{3} \frac{w_i}{\rho_{true,i}}.$$  

(7)

Thus, equations 5-7 enable us to obtain the porosity of tablets from THz measurements.
3. Results and Discussion

We used the real part of the effective refractive index, \(n_e\), obtained from the phase of the complex transmission coefficients to characterise the tablets. The computation time required to determine \(n_e\) for a complete spectrum consisting of 251 frequency points was about one second. Fig. 2a shows the comparison of the measured phase of relative transmission with the model presented in equation 1 for three tablets with the same API and filler particle size, and API concentration (experiment number 2 in table 1) but three compaction forces, \(F_1 = 8\) kN, \(F_2 = 12\) kN, \(F_3 = 16\) kN. The good agreement with the measurements validates the model. Fig. 2b shows the obtained effective refractive index of the three tablets over frequency. As can be observed, increasing compaction force increased the effective refractive index because higher compaction force reduces air voids in between tablet particles, increasing the effective refractive index. The minor oscillations observed in \(n_e\) were due to standing waves within the measurement set-up and the fact that we used the measured tablet thickness and not the effective tablet length, which in practice can have small discrepancies due to possible tablet inhomogeneities or beam properties.

Figure 2: a) Phase of relative transmission for tablets (experiment number 2 in table 1) with three compaction forces, \(F_1 = 8\) kN, \(F_2 = 12\) kN, \(F_3 = 16\) kN, showing a good agreement between model and measurement data b) Real part of effective refractive index over frequency. Higher compaction force increased the effective refractive index.

To study the effect of the varied design factors on the effective refractive index of tablets, the mean value of the effective refractive index across the frequency band was chosen as a response. The results were analyzed using a sta-
The modification of THz porosity with respect to design parameters, a) compaction force, b) API concentration, and c) filler particle size are shown, respectively. Plots are created from fitted first-order and second-order polynomials, similar to equation 8. In each plot, the line shows the THz porosity and the shaded area shows the standard deviation.

The effect of filler particle size on porosity is shown in Fig. 5c. It was observed that increasing particle size of the filler first results in a slight increase in porosity for filler particle size lower than 150 μm and then a decrease in porosity for larger particles. This behavior can be explained by particle fragmentation under compaction force during the tableting process. Mannitol (Tarlier et al., 2018) and Ibuprofen (Liu et al., 2008) are needle shape particles, which show friable deformation behavior under high compression pressure (Tarlier et al., 2018), (Le et al., 2006). Furthermore, there is a greater tendency for the larger granules to fragment under high compression pressure and therefore create closer packing and consolidation of the particles after fragmentation (Alderborn and Nyström, 1985), which results in lower porosity. Scanning electron microscopy photographs of the cross-section of one tablet (experiment number 3 in the table 1) were taken for investigating the fragmentation of the particles. As can be seen in Fig. 6, the results showed a particle size reduction down to around 10 μm, which verified the fragmentation deformation behavior of Mannitol and Ibuprofen.
4. Conclusion

We explored the THz-FD technique for fast porosity measurement of pharmaceutical tablets using a vector network analyzer. The effective refractive index of tablets was extracted from transmission measurements and transformed to the tablet porosity by an empirical linear correlation between tablet density and effective refractive index. We used design of experiments to investigate the applicability of the THz-FD technique to study the effect of factors such as API and filler particle size, API concentration, and compaction force on the porosity. The results showed that the THz-FD technique can detect and quantify changes in the tablet porosity, showing that the filler particle size and compaction force had a major impact on the effective refractive index and, consequently, porosity. Particle fragmentation was observed in the measurement results and verified with scanning electron microscopy. The extraction of tablet porosity from VNA measurements can be further refined using all four S-parameters (Bourreau et al., 2006), and also opens up for calibrated and traceable measurements (Ridler et al., 2019). This work showed that the THz-FD technique is promising for fast, non-destructive, and sensitive porosity measurements of pharmaceutical tablets. Moreover, the possibility to miniaturise terahertz sensors based on electronic solutions opens up for future compact porosity measurement systems.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table S1: List of the characterized tablets in this study. The ingredients were Ibuprofen supplied by IOL Chemicals and Pharmaceuticals (Punjab, India), Mannitol Parteck M100 and Mannitol Parteck M200 from Merck KGaA (Darmstadt, Germany), Mannitol Pearlitol 400DC from Roquette (Lestrem, France), Magnesium stearate from AstraZeneca R&D (Södertälje, Sweden). The thickness of each tablet was measured five times by a micrometer. Tablet density was calculated from the weight and dimensions of tablets, and the true density of the compact powder was calculated using equation 7.

| Tablet | Thickness (mm) | Mass (mg) | Tablet density (g cm\(^{-3}\)) | True density (g cm\(^{-3}\)) | API concentration (w/w %) | Compaction force (kN) |
|--------|----------------|-----------|-------------------------------|-------------------------------|---------------------------|------------------------|
| Set 1  |                |           |                               |                               |                           |                        |
| 1      | 3.340          | 306       | 1.166                         | 1.433                         | 16.8                      | 7.4                    |
|        | 3.190          | 306       | 1.221                         | 16.8                          | 12.2                      |                        |
|        | 3.106          | 306       | 1.254                         | 16.8                          | 16.0                      |                        |
| 2      | 3.325          | 304       | 1.164                         | 1.436                         | 16.2                      | 7.9                    |
|        | 3.175          | 304       | 1.219                         | 16.2                          | 12.1                      |                        |
|        | 3.089          | 304       | 1.253                         | 16.2                          | 15.9                      |                        |
| 3      | 3.072          | 303       | 1.256                         | 1.432                         | 16.0                      | 8.0                    |
|        | 2.976          | 303       | 1.296                         | 16.0                          | 11.8                      |                        |
|        | 2.926          | 303       | 1.318                         | 16.0                          | 15.8                      |                        |
| 4      | 3.095          | 305       | 1.255                         | 1.431                         | 16.2                      | 8.4                    |
|        | 3.015          | 305       | 1.288                         | 16.2                          | 11.9                      |                        |
|        | 2.956          | 305       | 1.314                         | 16.2                          | 15.9                      |                        |
| Set 2  |                |           |                               |                               |                           |                        |
| 5      | 3.298          | 303       | 1.170                         | 1.425                         | 18.5                      | 8.2                    |
|        | 3.174          | 303       | 1.216                         | 18.5                          | 12.2                      |                        |
|        | 3.076          | 303       | 1.254                         | 18.5                          | 15.8                      |                        |
| 6      | 3.325          | 306       | 1.161                         | 1.427                         | 18.0                      | 7.9                    |
|        | 3.203          | 306       | 1.216                         | 18.0                          | 12.0                      |                        |
|        | 3.121          | 306       | 1.248                         | 18.0                          | 15.9                      |                        |
| 7      | 3.121          | 306       | 1.248                         | 1.421                         | 18.4                      | 8.2                    |
|        | 3.029          | 306       | 1.286                         | 18.4                          | 12.1                      |                        |
|        | 2.961          | 306       | 1.316                         | 18.4                          | 15.8                      |                        |
| 8      | 3.117          | 307       | 1.254                         | 1.424                         | 17.9                      | 8.5                    |
|        | 3.057          | 307       | 1.278                         | 17.9                          | 11.9                      |                        |
|        | 3.014          | 307       | 1.297                         | 17.9                          | 15.3                      |                        |
| Set 3  |                |           |                               |                               |                           |                        |
| 9      | 3.321          | 304       | 1.165                         | 1.416                         | 20.6                      | 8.2                    |
|        | 3.180          | 304       | 1.217                         | 20.6                          | 12.2                      |                        |
|        | 3.103          | 304       | 1.247                         | 20.6                          | 16.0                      |                        |
| 10     | 3.371          | 307       | 1.160                         | 1.419                         | 19.9                      | 7.8                    |
|        | 3.250          | 307       | 1.203                         | 19.9                          | 11.7                      |                        |
|        | 3.146          | 307       | 1.242                         | 19.9                          | 15.4                      |                        |
| 11     | 3.066          | 302       | 1.254                         | 1.417                         | 19.5                      | 8.0                    |
|        | 2.985          | 302       | 1.288                         | 19.5                          | 11.9                      |                        |
|        | 2.972          | 302       | 1.294                         | 19.5                          | 15.2                      |                        |
| 12     | 3.144          | 306       | 1.239                         | 1.418                         | 19.3                      | 8.4                    |
|        | 3.054          | 306       | 1.276                         | 19.3                          | 12.0                      |                        |
|        | 3.008          | 306       | 1.295                         | 19.3                          | 16.0                      |                        |
| Set 4  |                |           |                               |                               |                           |                        |
| 13     | 3.335          | 304       | 1.161                         | 1.407                         | 22.7                      | 8.3                    |
|        | 3.195          | 304       | 1.212                         | 22.7                          | 11.9                      |                        |
|        | 3.133          | 304       | 1.236                         | 22.7                          | 16.1                      |                        |
| 14     | 3.336          | 304       | 1.160                         | 1.409                         | 22.2                      | 8.3                    |
|        | 3.230          | 304       | 1.198                         | 22.2                          | 11.8                      |                        |
|        | 3.129          | 304       | 1.237                         | 22.2                          | 15.6                      |                        |
| 15     | 3.124          | 303       | 1.235                         | 1.402                         | 22.9                      | 7.9                    |
|        | 3.012          | 303       | 1.281                         | 22.9                          | 13.0                      |                        |
|        | 2.973          | 303       | 1.298                         | 22.9                          | 16.0                      |                        |
| Tablet | Thickness (mm) | Mass (mg) | Tablet density (g cm$^{-3}$) | True density (g cm$^{-3}$) | API concentration (w/w %) | Compaction force (kN) |
|--------|---------------|-----------|-------------------------------|-----------------------------|---------------------------|----------------------|
| 16     | 3.154         | 305       | 1.231                         | 1.408                       | 21.4                      | 7.9                  |
|        | 3.071         | 305       | 1.264                         | 21.4                        | 11.7                      |                     |
|        | 3.041         | 305       | 1.277                         | 21.4                        |                           | 14.6                 |
| Set 5  |               |           |                               |                             |                           |                      |
| 17     | 3.348         | 304       | 1.156                         | 1.398                       | 24.8                      | 7.8                  |
|        | 3.215         | 304       | 1.204                         | 24.8                        | 11.8                      |                     |
|        | 3.151         | 304       | 1.228                         | 24.8                        |                           | 15.5                 |
| 18     | 3.375         | 307       | 1.158                         | 1.401                       | 24.1                      | 8.0                  |
|        | 3.270         | 307       | 1.195                         | 24.1                        | 11.5                      |                     |
|        | 3.154         | 307       | 1.239                         | 24.1                        |                           | 15.8                 |
| 19     | 3.142         | 304       | 1.232                         | 1.393                       | 25.0                      | 7.8                  |
|        | 3.050         | 304       | 1.296                         | 25.0                        | 12.1                      |                     |
|        | 3.021         | 304       | 1.281                         | 25.0                        |                           | 15.6                 |
| 20     | 3.148         | 305       | 1.234                         | 1.398                       | 23.8                      | 8.5                  |
|        | 3.064         | 305       | 1.267                         | 23.8                        | 12.3                      |                     |
|        | 3.036         | 305       | 1.279                         | 23.8                        |                           | 16.0                 |
| Center points |       |           |                               |                             |                           |                      |
| 21     | 3.372         | 309       | 1.167                         | 1.419                       | 20.0                      | 8.7                  |
|        | 3.240         | 309       | 1.214                         | 20.0                        | 12.3                      |                     |
|        | 3.164         | 309       | 1.244                         | 20.0                        |                           | 16.1                 |
| 22     | 3.378         | 307       | 1.157                         | 1.418                       | 20.1                      | 8.3                  |
|        | 3.241         | 307       | 1.206                         | 20.1                        | 11.8                      |                     |
|        | 3.107         | 307       | 1.258                         | 20.1                        |                           | 16.7                 |
| 23     | 3.378         | 305       | 1.149                         | 1.417                       | 20.4                      | 7.9                  |
|        | 3.204         | 305       | 1.212                         | 20.4                        | 12.0                      |                     |
|        | 3.097         | 305       | 1.254                         | 20.4                        |                           | 15.9                 |