Piecewise Whittle estimator for trabecular bone radiograph characterization

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\section*{ABSTRACT}

Osteoporosis is a disease in which low bone mass and microarchitectural deterioration of bone tissue lead to increased bone fragility and a consequent increase in fracture risk. The objective of this paper is to develop and validate a new method to assess bone microarchitecture on radiographs. Taking into account the piecewise fractal nature of bone radiograph images, an appropriate fractal model (piecewise fractional Brownian motion) is used to characterize the trabecular bone network. Based on the Whittle estimator, a new method for calculating the Hurst exponent is developed to better consider the piecewise fractal nature of the data. Different estimators are used and compared to the proposed method to discriminate two populations composed of healthy controls and osteoporotic patients. Our findings demonstrate that the new estimator proposed here provides effective results in terms of discrimination of the subjects and is better adapted to bone radiograph image analysis.

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1. Introduction

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture [1]. The most common method for osteoporosis diagnosis is to estimate Bone Mineral Density (BMD) by dual-energy X-ray absorptiometry [2]. However, BMD alone represents only 60\% of fracture prediction. The characterization of trabecular bone microarchitecture has been recognized as an important factor and completes the osteoporosis diagnosis using BMD [3], but it cannot be routinely obtained by noninvasive methods and requires a bone biopsy with histomorphometric analysis. This is why several attempts have been made to characterize trabecular bone microarchitecture by noninvasive methods [4–6].

The main question is how to improve the early diagnosis of osteoporosis and judge the porosity of the bone on X-ray radiographs. For this purpose, different methods have been extensively explored; some of them present certain limitations and are still under investigation [7–9]. Many models have been proposed to characterize and estimate parameters linked to bone fragility in order to discriminate people with and without osteoporosis. For several years, many researchers have considered models for describing irregular processes that are relevant to this issue. The advent of fractals to describe complex structures in biology and medicine such as trabecular bone has been recognized as an effective tool [10–12]. Fractal objects are characterized by a high degree of complexity but also by self-similarity represented by a repetition of patterns or statistical properties over different scales. This property of self-similarity enables the characterization of complex images by a unique parameter: the fractal dimension \( D \). Among these models, the fractional Brownian motion (fBm) model has shown potential usefulness for the characterization of gray level images.

fBm has been shown to be well suited for the fractal analysis of trabecular bone texture on calcaneus radiographs [13–15]. Several studies have modeled the trabecular bone texture using fractals, but without considering the nature of the data (fractal or not fractal) and the adequacy of the fBm model for the characterization of bone texture on radiographs. An increasing number of papers provide a theoretical basis for calculating the fractal behavior of cancellous bone in radiographs, but to the best of our knowledge very few studies deal with the selection of the processing and calculation methods which can provide a consistent and reliable determination of the fractal dimension.
These empirical findings suggest that it is necessary to find suitable tools taking into account situations where the classical fBm model shows its limits. This is the case of generalized multifractal motion where $H$ can evolve over time [16]. However, this process does not have stationary increments. Another generalization of fBm was proposed and called fBm of order $n$ [17]. The $H$ parameter of this process varies between $n - 1$ and $n$, where $n$ is a positive integer. On double self-similarity, a first approach in this direction was proposed in [18] and was called fractal signature. But this approach has no established theoretical basis. Other approaches based on fBm models were proposed in [19,20]. They consist of filtering or generalizing the fBm from its structure function [21]. However, these models have a complex analytic definition, and some difficulties arise in the range of variation of the process parameters or in the choice of the filter. A new model known as asymptotic fBm enables short- and long-term correlation effects to be controlled independently [22]. However, the $H$ parameter which governs the long-term dependency can evolve only between 0.5 and 1. Moreover, the link between this model and fBm is not direct.

One of the present authors introduced a model called piecewise fractional Brownian motion model (p-fBm) which appears to be more appropriate for bone radiograph characterization [23]. The p-fBm model is governed by 3 parameters: $H_{0}$ at low frequencies, $H_{I}$ at high frequencies, and a cut-off frequency $\gamma$ which separates the two regimes. For $H_{0} = H_{I} = H$, the p-fBm process is reduced to the classical fBm. The p-fBm makes it possible to generalize the class of fBm signals and thus provides a more suitable tool for bone characterization. Indeed, as can be seen in Fig. 2, in a log–log scale, the Power Spectral Density (PSD) of the derivative of the lines of bone radiograph images presents two different fractal regimes.

The use of any model involves finding estimators for the parameters of the model. Different estimators have been used to calculate the $H$ parameter. Istas and Lang developed an efficient estimator (ILE) [24] based on the generalization of the quadratic variations of the Gaussian process; this estimator provides good results. The box counting [25,26] and the mathematical morphology methods [27] are based on the properties of geometric fractals. They consist in measuring a geometrical parameter at different scales, and regression in a log–log scale is then used to find a fractal dimension. These methods are biased, suffer from problems related to sampling and are not well suited for trabecular bone characterization [28]. Among the other techniques which provide promising results, the Wavelet Estimator (WE), a multi-scale approach, is efficient in terms of estimated average, but the variance is rather large [29,30]. In the frequency domain, two approaches can be deduced from the properties of the fBm model: the Brownian Spectral Estimator (BSE) and the Gaussian Spectral Estimator (GSE) [31]. These kinds of methods provide poor results due mainly to the non-stationary of the process. The second estimator (GSE) uses the increments of the fBm and provides better results than the BSE, both in terms of bias and of variance. In the temporal domain, the maximum likelihood estimator (MLE) [32] was proposed; it is based on the statistical properties of the fBm model. The MLE is theoretically efficient in terms of bias and variance and has demonstrated competitive performances. An efficient approximation of the MLE called the Whittle Estimator (WHe) in the frequency domain was developed in [33]. This method is fast and provides good results in terms of bias and variance. The objectives of this paper are twofold: first, to use a model better suited for the characterization of trabecular bone texture, namely, the piecewise fractional Brownian motion model (p-fBm) [23]; second, to propose a new variant of the efficient Whittle Estimator that is well adapted for p-fBm processes. This new estimator called the piecewise Whittle Estimator (p-WHe) makes it possible to estimate the two parameters $H_{0}$ and $H_{I}$ of the p-fBm. Our objective is to compare the p-WHe method to different estimators to discriminate two populations composed of 80 osteoporotic (OP) patients and 80 control (CT) subjects.

This paper is organized as follows: Section 2 presents the theory, where the classical fBm and the p-fBm models are introduced. The different estimators are also described. In Section 3, the comparison of different methods and the proposed estimator on trabecular bone texture is presented. The results are given in Section 4. A discussion and some conclusions with guidelines for further work are presented in Section 5.

2. Theory

This section presents the theory of the classical fractional Brownian motion model and introduces the piecewise fractional Brownian model.

2.1. Fractional Brownian motion model

fBm is a stochastic fractal process that models $1/f$ spectrum, long-range dependence, and self-similar behaviors developed by Mandelbrot and Van Ness [34] as a generalization of classical Brownian motion ($H = 0.5$) [34]. This process is governed by a unique parameter, the Hurst exponent $H (0 < H < 1)$ which is linked to the fractal dimension by $H = E + 1 − D$, where $E$ is the Euclidian dimension.

The spectral representation of fBm, $B_H(t)$ is given by [35]:

$$B_H(t) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} \frac{1}{(i\omega)^{H+1/2}} (e^{i\omega t} - 1) dB_H(\omega).$$

(1)

It is a Gaussian, continuous, centered, and non-stationary second-order process. With the initial condition $B_H(0)=0$, its covariance function, denoted $r$, is given by:

$$r_B(i,j) = E[B_H(i)B_H(j)] = \frac{\sigma^2}{2} \left( |i|^{2H} + |j|^{2H} - |i-j|^{2H} \right),$$

(2)

where $E[,]$ is the mathematical expectation, $a$ is a constant and $V_H$ a function of $H$ defined as [36]:

$$V_H = \Gamma(1-2H) \cos(\pi H) / \pi H.$$

(3)

where $\Gamma$ is the gamma function.

The main property of fBm is its statistical self-similarity, which means that the same properties can be observed at different scales. It is expressed as:

$$B_H(km) = k^H B_H(m); \quad \forall k \quad \text{and} \quad m > 0$$

(4)

As fBm is a non-stationary process, it is more convenient to study its increments, called fractional Gaussian noises ($fGn$), which are stationary. The $fGn$, $G_m$, is defined as the derivative of fBm at a resolution $m$:

$$G_m(i) = B_H(i) - B_H(i - m)$$

(5)

The covariance function, $r$, fully describes the $fGn$ process, with:

$$r_{G_m}(\tau) = E[G_m(i)G_m(i + \tau)]$$

$$= \frac{\sigma^2 m^{2H}}{2^{1+2H}} \left( |\tau + m|^{2H} - 2|\tau|^{2H} + |\tau - m|^{2H} \right)$$

(6)

where $\sigma^2 = \frac{\sigma}{2} V_H(m^{2H})$ is the variance of $G_m$. For $0 < H < 0.5$, the correlation is negative. For $H = 0.5$, this process is the Gaussian white noise; and for $0.5 < H < 1$, the correlation is positive. Moreover, for high values of $\tau$, the covariance function varies as $\tau^{2H-2}$. In this case we refer to long memory or long dependence processes [37].
The power spectral density (PSD) of the fGn can be calculated from Eq. (6), and when \( m \to 0 \), a normalized spectrum of the fGn can be defined [30]:

\[
\text{PSD}_{\text{fGn}}(f) \propto |f|^{1-2H}
\]  

(7)

In a log–log scale, the PSD of an fBm process is a line of slope (1 – 2H).

As shown in Section 3, for trabecular bone texture, the PSD presents several fractal regimes with different slopes, hence the interest of the piecewise fractional Brownian motion model (p-fBm) presented in the next section.

2.2. Piecewise fractional Brownian motion model

In classical fBm, the Hurst parameter \( H \) corresponding to one frequency regime describes the process completely, but a unique frequency regime or self-similar behavior is not sufficient for certain data observed since the process 1/f cannot be present in practice for both very low and very high frequencies. In practice, we study only a limited zone in 1/f. In some cases such as in bone radiographs, there is no, but two areas of fractal parameters: Ho for low frequencies and Hi for high frequencies. These two areas are separated by a cut-off frequency \( \gamma \). Such processes can be modeled by the p-fBm model, denoted \( B_{\text{Hi}} \), and defined by 3 parameters, \( Ho, Hi \) and \( \gamma \), \( 0 < Ho \leq 1, 0 < Hi < 1 \) and \( \gamma > 0 \). The p-fBm is given by:

\[
B_{\text{Hi},\gamma}(t) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} F_{\text{Hi},\gamma}(\omega)(e^{i\omega t} - 1)dB(\omega)
\]

(8)

where

\[
F_{\text{Hi},\gamma}(\omega) = \begin{cases} 
1_{(|\omega|)}(\omega) & \text{if } \gamma is between} \gamma_{H} - \gamma_{H} \\
\frac{1}{|\omega|^{\gamma_{H} - \gamma_{H}}} & \text{otherwise}
\end{cases}
\]

(9)

1(\omega) is the indicator function over the interval \( I \) (i.e. \( 1(\omega) \equiv 1 \) if \( \omega \in I \), \( 1(\omega) \equiv 0 \), otherwise). The continuity in \( \gamma \) is ensured by the factor \( \gamma_{H} \). p-fBm is a Gaussian, continuous and non-stationary process. When \( H = Ho = Hi \), the p-fBm is reduced to the classical fBm of parameter \( H \).

As for fBm, the increment processes of p-fBm, denoted by \( C_{\text{Hi},\gamma} \), and called piecewise fractional Gaussian noises (p-fGn), are defined as:

\[
C_{\text{Hi},\gamma}(t) = B_{\text{Hi},\gamma}(t + u) - B_{\text{Hi},\gamma}(t)
\]

(10)

where \( u \in R \) is fixed. Their covariance \( r_{\text{Hi},\gamma}(\tau) \) is given by [23]:

\[
r_{\text{Hi},\gamma}(\tau) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} 2 \sin \left( \frac{\omega \tau}{2} \right) \\
\times \sin \left( \frac{\omega u}{2} \right) e^{i\omega \tau} F_{\text{Hi},\gamma}(\omega)^2 d\omega.
\]

(11)

when \( u = v \), the PSD of the p-fGn is:

\[
\text{PSD}_{\text{Hi},\gamma}(\omega) \propto 4 \sin^2 \left( \frac{\omega u}{2} \right) |F_{\text{Hi},\gamma}(\omega)|^2
\]

(12)

The p-fBm process has two asymptotic self-similarity regimes [23]. For a large scale of observation, the process behaves like a self-similar process with parameter Ho, and for a closer scale of observation, the process is governed by the self-similar parameter Hi.

2.3. Estimators of the \( H \) parameter

Different estimators have been used to estimate the \( H \) parameter of the fBm. They are divided into temporal, multi-scale, spectral, and fractal-geometry-based groups and differ in bias and variance of the results produced. Our objective is not to present an exhaustive list of the different estimators but rather to demonstrate the relevance of our proposed method to access osteoporosis on bone radiographs. For this reason we have chosen four estimators commonly used by the scientific community which provide efficient results in terms of discrimination of different populations for bone diagnosis.

2.3.1. Istsas and Lang Estimator (ILE)

The ILE was developed by Istsas and Lang [24] and is based on the generalization of the quadratic variations of the Gaussian process. If \( (B_{H}(p/N))_{p=0, N} \), denotes the discretized fBm process, the quadratic variation of the process is given by:

\[
\hat{V}_H = \sum_{p=0}^{N-1} \left( B_H \left( \frac{k+1}{N} \right) - B_H \left( \frac{k}{N} \right) \right)^2
\]

(13)

Guyon and Léon [38] have shown that \( N^{2H-1} \hat{V}_H \) converges asymptotically to a strictly positive deterministic constant \( c \) when \( N \to +\infty \); therefore,

\[
\hat{H}_H = \frac{1}{2} \left( 1 + \log \frac{\hat{V}_H}{\log N} \right)
\]

(14)

converges asymptotically to \( H \) when \( N \to +\infty \). In order to obtain a standard Central Limit Theorem for all the values of \( H \), Istsas and Lang proposed replacing the Quadratic Variation \( \hat{V}_H \) by a Generalized Quadratic Variation (GQV). For example,

\[
\hat{V}_N = \sum_{p=0}^{N-2} \left( B_{H} \left( \frac{p+2}{N} \right) - 2B_{H} \left( \frac{p+1}{N} \right) - B_{H} \left( \frac{p}{N} \right) \right)^2
\]

(15)

By making use of GQV, Istsas and Lang constructed asymptotically normal estimators of Hurst exponents for a wide class of Gaussian stationary increment processes, which includes fBm.

2.3.2. Wavelet-based Estimator (WE)

Wavelet-based approaches are used in several domains and have provided efficient results. Wavelet decomposition shows that the non-stationarity of the process is found only in the low frequency signal. The signals of the details are stationary and decorrelated [30]. When split to dyadic wavelets, the variance of details \( d_j \) at a scale \( j \) follows the law:

\[
\text{Var}(d_j) \propto (2^j)^{2H+1}
\]

(16)

and

\[
\text{Log}_{2}(\text{Var}(d_j)) \propto -(2H + 1)j + \text{constant}
\]

(17)

The \( H \) parameter can be estimated by linear regression using Eq. (17). Any Daubechies wavelet [39] with more than two zero moments is suitable. For the effective implementation of this method, the edge effects due to filtering can result in wrong values. The polluted samples are ignored in calculations. To reduce these edge effects, we chose a wavelet as small as possible (a Daubechies wavelet with 4 coefficients).

2.3.3. fGn-based Spectral Estimator (GSE)

This method has the common characteristic of relying on the overall shape of 1/f spectra of the increments of the fBm. The final step is a regression in log–log scale to estimate the \( H \) parameter.

Eq. (7) shows that the PSD follows a law in \( |f|^{1-2H} \). In a log–log scale, the PSD function of the frequency is a line of slope \( 1 – 2H \). The \( H \) parameter can be estimated by linear regression. With regard to the implementation, the average spectrum is estimated by the square of the modulus of the Fourier transform obtained by the Fast Fourier Transform (FFT) algorithm.
2.3.4. Whittle Estimator (WhE)

In the temporal domain, the maximum likelihood estimator (MLE) [32] is based on the statistical properties of the fBm model. This estimator provides efficient results in terms of bias and variance. Nevertheless, for medical applications, it is preferable to use fast algorithms with real time execution. The MLE method is time and memory consuming and is hence hardly applicable for large sized samples. For these reasons an efficient approximation called Whittle in the frequency domain was developed [33] which is asymptotically efficient for the increments of fBm [40]. The Whittle approximation of the Likelihood Function (LF) calculates the LF in the spectral domain. It involves looking for the minimum distance between the spectra of the characterized process and that of the theoretical model. If $x$ is the vector of increments supposed to be an fGn, the Whittle Likelihood Function (WLF) of $x$ can be written in the discrete case as [37]:

$$\text{WLF}(x; H, c) = \sum_{j=1}^{[m]} \left( -\ln[T(j; H, c)] + \frac{P(j)}{T(j; H, c)} \right)$$  \tag{18}$$

where $[m]$ is the integer part of $(N-1)/2$, $T$ is the theoretical power spectral density of the fGn process, $P$ is the periodogram of the vector $x$ and $c$ is a proportionality constant.

To find the maximum of the WLF function, $T$ is decomposed as $cT'$ and taking the derivative relative to $c$ to zero, we get:

$$c = \frac{\sum_{j=1}^{[m]} P(j)}{\sum_{j=1}^{[m]} T(j; H)}$$  \tag{19}$$

The $H$ parameter estimated by the WhE, $\hat{H}_{\text{WE}}$ is given by:

$$\hat{H}_{\text{WE}} = \max_{0 < H < 1} \left\{ \sum_{j=1}^{[m]} \left( -\ln(cT'(j; H)) - \frac{P(j)}{cT'(j; H)} \right) \right\}$$  \tag{20}$$

$T$ can be calculated from the PSD of the fGn or as the Fourier transform of the covariance matrix of the fGn. The computational complexity of the WhE is $O(N\log N)$ and the memory required is $O(N)$, which is more convenient than the classical MLE.

2.3.5. Piecewise Whittle Estimator (p-WhE)

Contrary to fBm which is governed by a unique parameter, $H$, p-fBm is governed by 3 parameters: Ho for low frequencies, Hi for high frequencies, and $\gamma$, a cut-off frequency which separates the two regimes. Taking into account the two regimes and based on the classical Whittle Estimator, we propose a new estimator that is more convenient for p-fBm processes, the piecewise Whittle Estimator (p-WhE). In this case, the piecewise Likelihood Function (pWLF) to be minimized is:

$$\text{pWLF}(x, H, Hi, \gamma, c_0, c_1) = \sum_{j=1}^{\gamma} \left( -\ln[To(j; Ho, c_0)] - \frac{Po(j)}{To(j; Ho, c_0)} \right) + \sum_{j=\gamma}^{[m]} \left( -\ln[Ti(j; Hi, c_1)] - \frac{Pi(j)}{Ti(j; Hi, c_1)} \right)$$  \tag{21}$$

To find the maximum of the pWLF function, To and Ti are decomposed as $c_o To$ and $c_i Ti$ respectively. Taking the derivatives relative to $c_o$ and $c_i$ to zero, we get in low frequencies:

$$c_o = \frac{\sum_{j=1}^{\gamma} Po(j)}{\sum_{j=1}^{\gamma} To(j; Ho)}$$  \tag{22}$$

and in high frequencies:

$$c_i = \frac{\sum_{j=\gamma}^{[m]} Pi(j)}{\sum_{j=\gamma}^{[m]} Ti(j; Hi)}$$  \tag{23}$$

The Ho and Hi parameters estimated by the maximum likelihood of Whittle (p-WhE) are:

$$\hat{H}_o = \max_{0 < Ho < 1} \left\{ \sum_{j=1}^{\gamma} \left( -\ln(c_o To(j; Ho)) - \frac{Po(j)}{c_o To(j; Ho)} \right) \right\}$$  \tag{24}$$

$$\hat{H}_i = \max_{0 < Hi < 1} \left\{ \sum_{j=\gamma}^{[m]} \left( -\ln(c_i Ti(j; Hi)) - \frac{Pi(j)}{c_i Ti(j; Hi)} \right) \right\}$$  \tag{25}$$

The cut-off frequency $\gamma$ corresponds to the peak of the periodogram (Fig. 2d) and is computed as the maximum of the global periodogram including the low and the high frequencies. To’ and Ti’ can be calculated from the PSD of the fGn or as the Fourier transform of the covariance matrix of the fGn, in low frequencies (for To’) and in high frequencies (for Ti’). In the next section, we give further details of the proposed approach to estimate Ho and Hi parameters on bone radiograph images.

3. Application to bone radiographs

This section describes the protocol of the clinical study, the data acquisition and the application of the described methods to characterize the data. Two populations composed of osteoporotic (OP) patients and control (CT) subjects were involved in this study.

3.1. Subjects

All the OP patients (fracture cases) and CT subjects voluntarily entered the study after written informed consent. Patients were systematically screened from all women attending the bone densitometry unit for routine clinical care and from patients hospitalized in the rheumatology, orthopedic and geriatric units. For each fracture case recruited, we enrolled control cases paired for age (±5 years) and Body Mass Index (BMI) (±2 kg/m²). This study involved 160 women, 80 controls aged 68.93±9.78 SD and 80 osteoporotic fracture cases aged 71.34±10.55 SD. BMI values were 25.73±4.10 SD and 26.21±4.38 SD for the CT and OP populations, respectively. No significant difference was found either for the age ($p$-value NS) or for the BMI ($p$-value NS).

All the patients filled out an osteoporosis risk questionnaire that included: age, personal and family history of fracture, tobacco (yes or no) and alcohol (yes or no) consumption, menopausal status (time since menopause), use of hormone replacement therapy (HRT) (yes or no, treatment duration), treatment by oral corticosteroids (yes or no, dose and duration), other medication and other diseases (rheumatoid arthritis, etc.). Participants were also asked if they needed to use their arms to assist themselves in standing up from a sitting position and what physical activity they took (less or more than two hours per week for the following activities:
walking, gardening, sport, etc.). Patients treated with corticosteroids, fluoride, bisphosphonates, HRT, or calcitomin for more than six months in the previous year were excluded from the study. We also excluded patients with known diseases which could interfere with bone metabolism: osteomalacia, bone cancer, myeloma, Paget’s disease, hyperparathyroidism, severe renal or hepatic insufficiency, prolonged immobilization (more than two months in the previous year). CT cases were excluded in the case of treatment or disease which could interfere with bone metabolism.

3.2. Image acquisition

Images were obtained on calcaneus bone with a direct digital X-ray prototype (BMA™, D3A Medical Systems, Orleans, France) [13]. We used the calcaneus because of the limited soft tissues surrounding this bone. Soft tissues could increase the variability of the method. The study of the calcaneus seems relevant because it contains 90% of trabecular bone [41] and is a good predictive site of fracture in terms of bone mineral density [41].

The devices for the study were cross-calibrated. The cross-calibration procedure has been described in [42]. The same radiographic parameters were used for the prototypes. Focal distance was set at 1.15 m. The X-ray parameters were 55 kV and 20 mAs for all patients. Scanning the heel permitted the selection of a similar measurement site (ROI) for each subject by using anatomical landmarks as previously described [43]. These anatomical landmarks were localized by the operator on the image, allowing positioning of the ROI (1.6 × 1.6 cm²) performed by the software device (Fig. 1). Then the H parameter which describes the texture was calculated using different approaches on the ROI to evaluate the bone microarchitecture quality.

Fig. 2 illustrates an example of a line extracted from a calcaneus texture ROI of a patient; we can notice the non-stationarity of the signal (Fig. 2b). As recalled above, the increments of fBm are easier to study due to their stationarity; this can be observed in Fig. 2c.

Bone trabeculae are organized so as to supply a mechanical resistance adapted to various constraints. Trabeculae in the directions undergoing weak constraints are less numerous and less thick. A precise analysis of the mean periodogram of the increments of the lines extracted from the ROI is presented in Fig. 2d. As can be seen, due to the complexity of the trabecular bone structure, the periodogram reveals two fractal areas separated by a cut-off frequency γ. Thus, the fBm model is not well adapted for the characterization of such data. For this reason we propose to employ the p-fBm model to better characterize these data. In this case, the first area, in the low frequencies, is governed by Ho, while the second area, in the high frequencies, is ruled by Hi.

4. Results

To demonstrate the efficiency of our approach to separate the two populations, the fBm and pBm models were used with the appropriate estimators. The fBm model was used with the ILE, WE, GSE and WhE methods, while the p-fBm model was used with our new proposed method p-WhE.

All the estimators (ILE, WE, GSE, WhE, p-GSE and p-WhE) were applied line by line with the same protocol for all the ROIs and the results were averaged to obtain a single measure corresponding to each image.

To highlight the fractal character and estimate the Ho and Hi parameters using the p-WhE method, two limited areas, Area 1 and Area 2 related to the low and high frequencies respectively were determined as Area 1 = [fimin, fimax] and Area 2 = [fimin, fimax]. These two areas are represented in Fig. 2d.

For practical implementation, γ was estimated automatically as the frequency corresponding to the maximum of the periodogram over the increments of the lines of each image. Following, the four frequencies fomin, fomax, finmin and finmax were selected from the linear regions Area 1 and Area 2, respectively. In a first time, these frequencies were selected manually from a first image of the database so as to capture a maximum of points in each linear region. Then, the selected frequencies were reused for the rest of the images of the database. This way, we ensure the estimation of the Ho and Hi parameters from the same regions. Finally, the p-WhE algorithm was applied to each image. Section 4.3 reports the effect of varying these frequencies on the results.

To enable comparison of the p-WhE method, we extended the GSE method to the p-fBm model. In this case, it consists in estimating the two parameters Ho and Hi in Area 1 and Area 2 respectively using linear regression as illustrated in Fig. 2d. For the following, this estimator is called p-GSE.

4.1. Comparison of the different estimators using the Wilcoxon test

The performance of an estimator to discriminate the two populations was evaluated with the p-value statistical test using the rank sum Wilcoxon test [44]. We considered a highly statistical significant p-value (p-value < 0.001). Table 1 presents the results expressed as mean ± standard deviation (SD) for all the subjects.

As can be seen in Table 1, all the estimators separated significantly the OP patients and the CT subjects. The obtained p-values, 7.99e-06, 3.0e-06, 7.16e-07 and 1.96e-07 respectively for ILE, WE, GSE and WhE with the classical fBm are quite acceptable, demonstrating that the fBm model has potential for the characterization of bone X-ray images.
Fig. 2. A representative ROI extracted from a calcaneus (a), a line extracted from the ROI (a) according to the arrow (b), the increments of the line presented in b (c), and the periodogram of the increments of the lines of the ROI (d).

The different mean values of the H parameter and the obtained standard deviations are presented in Fig. 3. The boxes represent 95% confidence intervals of the values. Some overlapping between the subjects (CT and OP) can be observed for the different estimators, except with the p-WhE method where a relatively good separation and a small overlap are obtained with the Hi parameter measured in the high frequency domain.

4.2. Comparison of the different estimators using the Receiver Operating Characteristic

To compare the performances of the p-WhE technique to the other methods, the Receiver Operating Characteristic (ROC) analysis was performed on the results of our experiments [45] (Fig. 4). Using the fbm model with the ILE, WE, GSE and WhE; and the pfbm model with the p-WhE and p-GSE, the properties of the ROC curves were calculated for each discriminant estimator. The significance level of each parameter was studied following the technique described by Hanley and McNeill [45]. SE (Standard Error) gives the standard error of the measure, TP (True Positive) is the number of OP people correctly identified, FP (False Positive) is the number of CT people incorrectly identified, TN (True Negative) is the number of CT people correctly identified, FN (False Negative) is the number of OP people incorrectly identified, Sn (True positive rate or sensitivity) as Sn = TP/(TP+FN) is the test's ability to identify positive results, Sp (Specificity or True Negative Rate) as Sp=TN/(FP+TN) is the

<table>
<thead>
<tr>
<th>Model</th>
<th>Estimator</th>
<th>CT Hmean ± SD</th>
<th>OP Hmean ± SD</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>fbm</td>
<td>ILE</td>
<td>0.858 ± 0.053</td>
<td>0.808 ± 0.072</td>
<td>7.99e-06</td>
</tr>
<tr>
<td></td>
<td>WE</td>
<td>0.690 ± 0.063</td>
<td>0.639 ± 0.064</td>
<td>3.05e-06</td>
</tr>
<tr>
<td></td>
<td>GSE</td>
<td>0.688 ± 0.040</td>
<td>0.649 ± 0.048</td>
<td>7.16e-07</td>
</tr>
<tr>
<td></td>
<td>WhE</td>
<td>0.770 ± 0.042</td>
<td>0.723 ± 0.055</td>
<td>1.96e-07</td>
</tr>
<tr>
<td>p-fbm</td>
<td>p-GSE (Ho)</td>
<td>-0.393 ± 0.405</td>
<td>-0.405 ± 0.202</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>p-GSE (Hi)</td>
<td>1.356 ± 0.105</td>
<td>1.221 ± 0.126</td>
<td>2.21e-10</td>
</tr>
<tr>
<td></td>
<td>p-WhE (Ho)</td>
<td>0.847 ± 0.017</td>
<td>0.839 ± 0.017</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>p-WhE (Hi)</td>
<td>0.786 ± 0.003</td>
<td>0.781 ± 0.003</td>
<td>1.46e-13</td>
</tr>
<tr>
<td></td>
<td>γ</td>
<td>0.345 ± 0.053</td>
<td>0.372 ± 0.057</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Table 1
Mean ± SD of the H parameter estimated by the different estimators for OP patients and CT subjects as well as p-values test. A p-value is considered as statistically significant if p-value < 0.001.
Fig. 3. Hurst exponents ± SD estimated using ILE, WE, GSE and WhE (a), p-GSE (b) and p-WhE (c) for the CT and OP groups. The boxes represent 95% confidence intervals of the values.

ability of the test to identify negative results, PPV = TP/(TP + FP) is the percentage of the Positive Predictive Value or accuracy for positive prediction, NPV = TN/(TN + FN) is the percentage of the Negative Predictive Value or accuracy for negative prediction, AUC is the Area Under the ROC Curve and ACC = (TP + TN)/(TP + FP + TN + FN) is the Accuracy of discrimination or Classification of the subjects.

The confusion matrices are shown in Table 2. The results obtained with the different estimators of classical fBm show that the WhE performs better with the highest AUC value and with minor false detections. The development of a new variant of the WhE to obtain better results and enhance the classification rate is therefore meaningful.

A sensitivity of 100% of the p-WhE for the diagnosis of osteoporosis was obtained at Hi = 0.7871. A specificity of 100% was reached at Hi = 0.7804. The best compromise between Sn and Sp was located at the crossover point of the two parameters, i.e., at Hi = 0.7838 with 18 FN and 20 FP cases (Sn = 77% and Sp = 75%). Below the value Hi = 0.7804, only OP patients were found, corresponding to a specificity of 100%. The analysis of the AUC shows that for these data, the p-WhE method performs better than the other estimators in the high frequencies for the diagnosis of osteoporosis. However, using the low frequencies (Ho) as well as the
frequency-cut (γ), we could not discriminate the two populations with p-WhE method.

Finally, comparing all the estimators, our proposed estimator provides the best performance in terms of statistical significance (p-value = 1.46e–13) and AUC (0.84).

As can be seen, using an appropriate model (p-fBm) with the proposed estimator (p-WhE), it is possible to increase the performances. The Hi value estimated in the high frequencies gives the best results in terms of classification rate and false detection.

As explained in Section 3.1, no significant differences were found between the two populations either for age or for BMI. However, a statistically significant difference (p-value = 5.3e–07) was found while measuring Bone Mineral Density (BMD). We found, 0.836 ± 0.119 SD for CT subjects and 0.732 ± 0.137 SD for OP patients.

To compare average values of Hi estimated using the p-WhE for CT and OP cases with adjustment for age, BMI and BMD, analysis of covariance (ANCOVA) was performed. The Pearson correlation coefficient, r was used for correlation analysis. Results (Table 3) demonstrate that adjustments of age, BMI and BMD, do not affect the performances of the Hi parameter (p-value < 0.0001) for separating the two populations.

4.3. Effect of the range of Area 1 and Area 2

In this section, we study the influence of the range of Area 1 and Area 2 on the robustness of the p-Whittle estimator. These two areas are limited, respectively by the frequencies (f_{min}, f_{max}) and (f_{min}, f_{max}). For this purpose, Area 1 and Area 2 were modified by varying the values of the frequencies (f_{min}, f_{max}) and (f_{min}, f_{max}) respectively around the frequency cut γ. As can be seen in Table 4, varying the range of Area 1 and Area 2 affects slightly the obtained p-values when trying to distinguish between the two populations. The Hi parameter still enables distinguishing between the two populations. The highest obtained p-value is lower than the lowest value obtained with the others methods (Table 1). This reinforces the robustness of our proposed method and its discriminating power.

5. Discussion

In this paper we have presented an efficient application of fractional Brownian motion (fBm) to bone texture images on X-ray radiographs. For this purpose, among different available models, we have selected piecewise fractional Brownian motion (p-fBm) as the most appropriate one. Unlike fBm, p-fBm is governed by 3 parameters: Ho at low frequencies, Hi at high frequencies, and a cut-off frequency γ which separates the two regimes. In a log–log scale, the PSD of the increments of the lines of bone radiograph images is composed of two fractal regimes and is similar to that of the target process, p-fBm (Fig. 2d).

The use of a model requires the development of adequate estimators of the model parameters. In our case, the estimator has to be efficient in terms of bias and variance and must consider the three model parameters. For this purpose, we have proposed a new variant of the efficient Whittle method, the piecewise Whittle Estimator (p-WhE). This new variant enables the three parameters of the p-fBm model to be estimated.

The p-WhE method was compared to different fractal estimators in the medical imaging field on trabecular bone radiographs. 160 gray level images, half from control subjects and half from osteoporotic patients were used for a clinical study.

Using the ROC curves and cross validation process to evaluate the classification accuracy. Our proposed approach has shown better separation between the osteoporotic cases and the healthy controls. Results were improved from a 74.9% classification rate with the classical Whittle estimator up to 84% of Area Under Curve (AUC) with the p-fBm model and our new proposed estimator.

<table>
<thead>
<tr>
<th>f_{min}</th>
<th>f_{max}</th>
<th>Test</th>
<th>p-Value</th>
<th>AUC</th>
<th>ACC</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>1</td>
<td>γ + 5</td>
<td>0.006</td>
<td>0.62</td>
<td>0.58</td>
</tr>
<tr>
<td>5</td>
<td>1.46e–13</td>
<td>γ + 5</td>
<td>0.006</td>
<td>0.62</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Table 4

Obtained p-values, AUC and ACC with the p-WhE method while varying the range of area 1 and area 2.
p-Whe. Moreover, the p-Whe is more accurate in detection rates (ACC = 0.76) and provides the lowest error (SE = 0.031).

Our study is strengthened by examining the p-value statistical test, results demonstrated that with the p-fbm model and our new proposed estimator, a highly statistically significant p-value was obtained. The comparison of our proposed estimator to a spectral based estimator derived from the p-fbm model on trabecular bone images still demonstrates that our proposed method is more effective and performs better for the classification of the two populations, while based on the estimation of the parameters in the same areas.

As can be noticed in Table 1, while dealing with the estimation of the H parameter, different p-values were obtained with the different estimators. This is mainly due to the properties of the characterized data which do not correspond completely to those of the target process, the fractional Brownian motion model. Moreover, as expected, there is agreement with all the previously mentioned studies and others [32,46,47] in that a lower H value is observed in the OP group than in the CT group.

Using the appropriate p-fbm model and the p-GSE method, we were able to improve the separation rate with the Hi parameter measured in the high frequency area (p-value = 2.21e−10). This result shows that the p-fbm model is better suited for the characterization of trabecular bone radiographic images. Nevertheless, the discrimination was poor with Hi measured in low frequencies (p-value = 0.6).

With the p-Whe method, a highly statistically significant p-value (p-value = 1.46e−13) outperforming the previous results was obtained in the high frequencies with the Hi parameter. This result is in accordance with our expectation as the evolution of architecture in osteopenia occurs in variations at scales that match our images at high frequencies, whereas there was a weak statistical significance between OP patients and CT subjects in the low frequencies (p-value = 0.006).

A weak greater p-value was found with the cut-off frequency γ meaning that the two regimes for the two populations are quite similar and do not separate the two populations.

The robustness of our proposed estimator was reinforced by varying the range of the frequencies used to estimate the Hi and Ho parameters and testing its ability to distinguish between the two populations. Results (Table 4) demonstrated that it is still possible to significantly distinguish between the two populations.

In this work, the H parameter was lower in the osteoporotic population than in the control one (Table 2). The same trend concerning the decrease in H was observed in previous clinical studies. This finding was observed for all the tested estimators, indicating that bone alterations are characterized by an increase in the fractal dimension. This increase is generally considered in terms of image analysis as a reflection of the increase in the roughness of the image. It could correspond to architectural disorganization of the trabecular network with osteoprosis.

A large variety of texture analysis methods have been proposed over the last three decades [48–50]. These methods are tested over textured surfaces which are quite distinctive for the human vision system. The textures present in osteoporotic and healthy bone radiographs, however, are visually close to each other, making the discrimination task very challenging. For clinical applications, automatic or semi-automatic processes are always preferred. A non stationary model like the pfbm is parameter independent, and therefore, there is no need of tuning the parameters, nor necessary processing of the data, the analyses are performed right away on the raw data. This is an important and positive point for the use of such model in the clinical routine.

Other techniques of microarchitecture evaluation are under investigation. Perpendicular QCT (pQCT), High Resolution pQCT (HRpQCT) and MRI have the advantage of evaluating directly the 3D properties of bone. However, their development is much less advanced [51,52], and there are as yet no large population studies. Furthermore, they are more costly, less accessible, and pQCT has the problem of higher radiation levels [53].

In conclusion, the combination of an adequate model and estimators to describe challenging textures such as trabecular bone on X-ray radiographs seems to be promising for medical applications. Fractal analysis of bone texture on calcaneus radiographs constitutes a simple low-radiation assessment of bone status. This noninvasive analysis may provide additional information about the trabecular microarchitecture to complete the diagnosis based on bone mineral density (BMD), leading to a better evaluation of fracture risk than with BMD alone. This is a new opportunity to improve the diagnosis of bone diseases such as osteoporosis.

We are currently investigating the exact synthesis of piecewise fractional Brownian images to validate the experimental behavior of our new proposed estimator compared to the classical ones.

Acknowledgments

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References


