

Evaluation of a Kalman-based block matching method to assess the bi-dimensional motion of the carotid artery wall in B-mode ultrasound sequences

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Abstract

We aim at investigating arterial diseases at early stage, by assessing the longitudinal (*i.e.* in the same direction as the blood flow) motion of the intima-media complex. This recently evidenced phenomenon has been shown to provide relevant and complementary information about vascular health.

Our method assesses the longitudinal and radial motion from clinical *in vivo* B-mode ultrasound sequences. To estimate the trajectory of a selected point during the cardiac cycle, we introduce a block matching method that involves a temporal update of the reference block using a pixel-wise Kalman filter. The filter uses the initial gray-level of the pixel as control signal to avoid divergence due to cumulating errors. The block and search-window sizes are adapted to the tissue of interest.

The method was evaluated on image sequences of the common carotid artery, acquired in 57 healthy volunteers and in 25 patients at high cardiovascular risk.

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Reference trajectories were generated for each sequence by averaging the tracings performed by three observers. Six different computerized techniques were also compared to our method.

With a pixel size of $30\ \mu\text{m}$, the average absolute motion estimation errors were $84 \pm 107\ \mu\text{m}$ and $20 \pm 19\ \mu\text{m}$ for the longitudinal and radial directions, respectively. This accuracy was of the same order of magnitude as the inter- and intra-observers variability, and smaller than for the other methods. The estimated longitudinal motion amplitude was significantly reduced in at-risk patients compared with healthy volunteers ($408 \pm 281\ \mu\text{m}$ vs $643 \pm 274\ \mu\text{m}$, $p < 0.0001$).

Our method can constitute a reliable and time-saving technique to investigate the arterial stiffness in clinical studies, in the objective to detect early-stage atherosclerosis.

Keywords: Carotid artery, Atherosclerosis, Speckle tracking, Block matching, Kalman filter, Longitudinal Motion, Cardiovascular Risk Marker

1. Introduction

1.1. Clinical context

Cardiovascular diseases represent the major cause of morbidity and mortality in middle- and high-income countries (WHO, 2011). Atherosclerosis, a syndrome affecting arterial blood vessels, is characterized by arterial wall stiffening and thickening, and potentially leads to thrombosis or stroke (Laurent et al., 2001). The common carotid artery (CCA, Fig. 1) being principally affected by this disease, it is widely considered for screening at early stage, that is to say before anatomical alteration such as the formation of atheromatous plaques (Gamble et al., 1994). The CCA consists of three concentric layers (*i.e.* intima, media and adventitia) around the lumen where the blood flows from the heart to the brain (Fig. 1).

Traditional risk markers focus on the two innermost layers thickening and stiffening. Carotid intima-media thickness (IMT) and its variation have been shown to have prognostic value for cardiac infarction and were also strictly correlated to the presence of coronary artery disease (Mutlu et al., 2011). Pulse wave velocity (PWV) was also demonstrated to represent an independent predictor of all-cause and cardiovascular mortality (Laurent et al., 2001). Arterial distensibility (*i.e.* cross-sectional diameter change) has been shown to be associated to cardiovascular risk in patients who already have vascular disease or atherosclerotic risk factors (Simons et al., 1999). However, the performance of these traditional risk markers as screening tests for sub-clinical atherosclerosis remains relatively poor (Simon et al., 2006).

On the other hand, the characterization of the arterial wall dynamics in the longitudinal plane, *i.e.* in the same axial direction as the blood flow, has only been little studied, although it is likely to further characterize the arterial compliance and may provide relevant and complementary clinical information about vascular health. Indeed, recent clinical investigations showed that the wall longitudinal motion was a predictor for cardiovascular accidents (Svedlund et al., 2011), was associated with the presence of cardiovascular risk factors (Ahlgren et al., 2009, 2012; Zahnd et al., 2011a), and was independent of established traditional risk markers while demonstrating a better screening potential (Zahnd et al., 2012).

As opposed to the radial motion (*i.e.* along the same direction as the cross-sectional diameter), the longitudinal motion remains more challenging to observe due to the homogeneity of the tissue layers in this direction (Fig. 1). The advances in the development of modern ultrasound (US) scanners have only recently lead to confirm the presence of the arterial longitudinal movement in an *in vivo* study (Persson et al., 2003). Please note that all along this article we use the term “longitudinal” to denote the direction of the blood flow, which is more or less horizontal in the images we

38 are dealing with, and the term “radial” to denote the direction perpendicular to
39 the blood flow (vertical). This vocabulary differs from the terms usually used in
40 the US imaging community, where “longitudinal” denotes the direction of the US
41 propagation, *i.e.* vertical the in B-mode images.

42 The objective of the present work is twofold. First, we introduce a novel tracking
43 method, dedicated to assess *in vivo* the cyclic longitudinal motion of the intima-media
44 complex, in US B-mode image sequences of the CCA acquired in clinical practice.
45 Second, we evaluate the accuracy of our method, and we present a comparison with
46 existing methods.

47 *1.2. Motion tracking in ultrasound image sequences of the CCA*

48 Bi-dimensional (2D, *i.e.* radial and longitudinal) motion estimation in US B-
49 mode image sequences can be assessed with a speckle tracking approach (Ophir et al.,
50 1991). This technique consists in estimating the displacement of an echo scatterer,
51 corresponding to a specific gray-level pattern, through the sequence.

52 *1.2.1. General principle of the block matching technique*

53 The speckle tracking is generally based on a block matching (BM, Fig. 2) frame-
54 work (Bohs and Trahey, 1991), in which the pattern to be tracked is represented by
55 a reference block \mathcal{B}_{ref} , *i.e.* a small image region encompassing the pattern. Given
56 a specified similarity criterion, the location of the pattern in the considered frame
57 is determined by seeking the best match between the reference block and candidate
58 blocks within a search window. The search window is usually defined by a maximum
59 displacement (margin) around the center \mathbf{p} of the best-matched block in the previ-
60 ously considered frame (Fig. 2). The motion of the pattern between two consecutive
61 frames is defined by the estimated displacement $\hat{\mathbf{d}}$ of the point \mathbf{p} , and the whole
62 trajectory through the sequence is calculated by summing up all the successively
63 estimated displacements.

64 *1.2.2. Challenges related to the tracking of the arterial wall longitudinal motion*

65 In our specific context, the *in vivo* estimation of the CCA wall longitudinal mo-
66 tion along several cardiac cycles in US B-mode imaging is hampered by three main
67 difficulties.

68 First, the tracked pattern, corresponding to the texture of the considered tissues,
69 presents a rather homogeneous profile in the longitudinal direction, with only a small
70 variation of the image gray level along the wall. This lack of contrast is caused by
71 the geometry of the anatomical structure of the vessel, consisting of layers aligned
72 along the longitudinal axis (Fig. 1). Moreover, the resolution cell of the ultrasound

73 scanner, corresponding to the spatial definition of the image, is generally coarser in
74 the direction perpendicular to the ultrasound beam than in the direction of the beam
75 propagation. This is due to the shape of the scanner’s point spread function (PSF):
76 its width, determined by the probe geometry as well as by the depth of the focal zone,
77 is most often larger than its height, determined by the ultrasound signal wavelength.
78 These two issues lead to the aperture problem, *i.e.* there is little evidence of the
79 longitudinal component of the motion.

80 Second, the small thickness of the region of interest, *i.e.* the IMT corresponding
81 roughly to half a millimeter, also represents a challenge. Indeed, while the tracked
82 block has to encompass a pattern sufficiently large to be discriminant, it should
83 not include the neighboring regions, lumen and adventitia, which have significantly
84 different characteristics. In particular, whereas adventitia is almost still, the blood
85 flow within the lumen is much faster than the intima-media motion to be estimated.

86 Third, the issue of speckle decorrelation, *i.e.* the degrading phenomenon caused
87 by out-of-plane movements, low echoes, tissue deformation and movement artifacts,
88 often leads to modifications of the tracked speckle pattern during the sequence. More-
89 over, the imaging quality corresponding to clinical routine can vary greatly between
90 different subjects, mostly due to the variability of the tissue echogenicity, and can
91 introduce blur or high noise. This issue, inherent to clinical US B-mode imaging, in-
92 deed represents a potential source of error for speckle tracking techniques, as it may
93 provoke a divergence in the trajectory estimation due to successive error cumulation.

94 1.2.3. Previous work related to the wall longitudinal motion

95 Recent work has contributed to characterize *in vivo* the specific longitudinal
96 motion of the human CCA wall in US B-mode image sequences, using different
97 speckle tracking approaches.

98 A first study (Golemati et al., 2003) used a traditional BM technique, with block
99 and window of dimensions, respectively, $3.20 \times 2.50 \text{ mm}^2$ and $4.50 \times 3.80 \text{ mm}^2$ (*i.e.*
100 margin 0.65 mm in both directions). This approach therefore considered a wide
101 region in the image, permitting *i)* to include a texture presenting a more contrasted
102 pattern in the longitudinal direction, and *ii)* to increase the robustness to the speckle
103 decorrelation issue. However the dimensions of the block were large in comparison
104 with the considered tissue thickness, possibly leading to a loss of precision. Indeed,
105 the investigated region, centered on the intima-media complex, also covered part of
106 the lumen and the adventitia tissues.

107 Another team proposed a different technique based on echo tracking (Persson
108 et al., 2003; Cinthio et al., 2005, 2006), focusing on a very local region of the image
109 with smaller block and window dimensions, respectively, $0.10 \times 0.10 \text{ mm}^2$ and $0.70 \times$

110 0.70 mm^2 (*i.e.* margin 0.30 mm in both directions). This approach also addressed
111 the issue of the lack of contrast of the longitudinal profile by tracking a single well
112 distinguishable scatter. Experimental *in vivo* trials showed high tracking accuracy,
113 and permitted a detailed analysis of the arterial longitudinal motion during the
114 cardiac cycle. From our experience however, such a small block size is sensitive to
115 noise, and would therefore not be well suited to clinical routine and large population
116 studies, where image quality varies from one subject to another.

117 Our team recently proposed a different approach, denoted as Multi-Block Match-
118 ing (MBM) (Zahnd et al., 2011a, 2012), aiming to assess the global motion of the
119 wall over a wide region of the intima-media complex by tracking multiple longitu-
120 dinally aligned points. The rationale of this framework is the following. First, the
121 speckle decorrelation issue is addressed by an Eulerian block matching approach.
122 This strategy involves an automatic and regular re-positioning of the blocks within
123 the intima-media complex in each frame of the image, using the *a priori* information
124 provided by the segmentation of the interfaces. In such manner, the drifting issue
125 that can occur when the tracked pattern is altered during the sequence is avoided,
126 as the motion of the tissues is assessed through a fixed window. Second, a series of
127 16 blocks is used to estimate the global motion of the entire length of the wall, in
128 order to increase the robustness of the method. Indeed, as some regions of the image
129 can temporarily suffer from noise during the sequence, the motion is assessed inde-
130 pendently by a block matching technique at regular position interval, and the final
131 resulting motion is determined by the median value of all estimates. Third, the di-
132 mension of the blocks and windows, respectively, $1.50 \times 0.30 \text{ mm}^2$ and $2.10 \times 0.90 \text{ mm}^2$
133 (*i.e.* margin 0.30 mm in both directions), aims to fit the morphology of the arterial
134 wall layers. This approach however may underestimate the amplitude of the actual
135 motion, as the median operation that is performed does not favor the displacement
136 values that are maximal.

137 A recent study (Gastouniotti et al., 2011) introduced a more robust speckle track-
138 ing scheme, in order to cope with the issue of speckle decorrelation by exploiting
139 a Kalman filtering approach (Kalman, 1960; Welch and Bishop, 1995). The block
140 and window dimensions used in that study were, respectively, $1.60 \times 1.00 \text{ mm}^2$ and
141 $2.90 \times 2.30 \text{ mm}^2$ (*i.e.* margin 0.65 mm in both directions). This promising work
142 showed that the use of Kalman filtering as an adaptive strategy to update either the
143 reference block or the 2D trajectory position permits to decrease the estimation error
144 generated by classical speckle tracking methods. However, the proposed approach
145 performs a scheme estimation *via* a fading memory system that does not involve a
146 control signal. Therefore, the divergence issue due to successive error cumulation
147 during the sequence remains as a potential source of error.

148 It is also noteworthy to mention that a different team recently proposed to use
149 the Velocity Vector Imaging commercial software (VVI, Research Arena 2; TomTec
150 imaging systems GmbH, Unterschleissheim, Germany), in order to investigate the
151 longitudinal motion amplitude of the carotid artery wall in several clinical stud-
152 ies (Svedlund and Gan, 2011; Svedlund et al., 2011).

153 *1.3. Objective and summary of the proposed approach*

154 Our work focuses on estimating the 2D trajectories (both the longitudinal and
155 radial components) representing the intima-media complex motion during the car-
156 diac cycle in US B-mode image sequences. The objective was to develop a method
157 capable of processing the sequences acquired in clinical practice as accurately as
158 human experts, while requiring significantly less effort and remaining more repro-
159 ducible. The goal of this article is to describe the developed method and to evaluate
160 it by comparing it with both reference trajectories traced by experts and with other
161 methods.

162 Our method is based on a Kalman-filtering scheme that performs the update
163 of the tracked reference pattern during the sequence, in the objective to cope with
164 speckle decorrelation issues. Namely, the Kalman filter estimates the gray levels
165 of the reference block \mathcal{B}_{ref} used within the speckle tracking framework. The main
166 originality of our approach resides in the use of a control signal, corresponding to the
167 initial state of the system $\mathcal{B}_{ref}(1)$, expected to avoid the divergence of the trajectory
168 across the cyclic motion of the tracked pattern. Indeed, this pattern, corresponding
169 to a local region of the tissues in the intima-media complex, generally undergoes an
170 alteration during the heart cycle. This alteration, due to the reasons explained in the
171 previous section, usually increases with the distance from the initial position. As the
172 observed motion is quasi-periodic, the region of interest is expected to periodically
173 recover its initial appearance when getting back close to the starting point. The
174 remaining characteristics of our method are the following. Firstly, we have chosen to
175 update each pixel of the reference block independently, so that localized variations of
176 intensity do not impact on the other pixels of the block. Secondly, the choice of the
177 block and search-window size was adapted to the arterial structure of interest and to
178 its motion. Namely, the block height and width respectively are slightly inferior to
179 the IMT and roughly equivalent to the empirically determined typical longitudinal
180 size of the tracked echoes, while the search window height and width were set such
181 that the margin corresponds to the maximum possible 2D displacement between two
182 consecutive frames.

183 The accuracy of our Kalman Block Matching (KBM) method was evaluated *in*
184 *vivo* on the carotid distal wall of 82 subjects (57 healthy volunteers and 25 at high

185 cardiovascular risk patients) in US B-mode sequences. The results of our method
186 were compared with those obtained manually by three experts, and differed from the
187 reference not more than the experts between them, while being fully reproducible.
188 A comparison was also carried out with six computerized methods representing the
189 main characteristics of the published work that investigated the wall longitudinal
190 motion. The KBM method demonstrated the highest accuracy. Finally, in the
191 aim to confirm the clinical relevance of the wall longitudinal motion estimated with
192 our KBM method, a comparison was performed between healthy volunteers and
193 at-risk patients. A statistical analysis showed that the amplitude of the estimated
194 longitudinal motion was significantly reduced in at-risk patients.

195 **2. Material and methods**

196 *2.1. Initialization phase*

197 In the first frame $\mathcal{I}(1)$ of the sequence, the user selects a single point $\mathbf{p}(1)$ within
198 the intima-media complex. The region that will be tracked with our KBM method
199 during the whole sequence is defined by a rectangular block \mathcal{B} centered on the initial
200 point, the size of which is well adapted to the wall anatomy. Preferably, the selected
201 point $\mathbf{p}(1)$ should correspond to a well distinguishable echo, *i.e.* to a bright local
202 scatterer contrasting with the surrounding uniform speckle texture, and is expected
203 to remain visually perceptible during the whole sequence (Fig. 3). This initialization
204 phase is very quick and easy, thanks to a smart implementation that allows the user
205 to preview the whole sequence and set the position of the desired initial point.

206 *2.2. Kalman filter*

207 We first provide a brief description of the Kalman filter theory, in order to intro-
208 duce the notations that are used in our specific implementation, which is subsequently
209 detailed.

210 *2.2.1. Theoretical background*

211 In a general manner, the Kalman filter (Kalman, 1960; Welch and Bishop, 1995)
212 provides the statistically optimal estimation $\hat{\mathbf{x}}$ of the state vector \mathbf{x} in a discrete
213 dynamic system governed by the following linear stochastic difference equation:

$$\mathbf{x}(n+1) = \mathbf{A}(n)\mathbf{x}(n) + \mathbf{B}(n)\mathbf{u}(n) + \mathbf{w}(n), \quad (1)$$

214 where $\mathbf{A}(n)$ is the state transition matrix, $\mathbf{B}(n)$ is the control matrix, $\mathbf{u}(n)$ is the
215 control signal, and $\mathbf{w}(n)$ is the process noise, white, with zero mean and covariance
216 matrix $\mathbf{Q}(n)$. It is assumed that the state $\mathbf{x}(n)$ cannot be directly assessed, instead
217 it is measured through an observation $\mathbf{z}(n)$, defined by:

$$\mathbf{z}(n) = \mathbf{H}(n)\mathbf{x}(n) + \mathbf{v}(n), \quad (2)$$

218 where $\mathbf{H}(n)$ is the observation matrix and $\mathbf{v}(n)$ is the observation noise, white, with
219 zero mean and covariance matrix $\mathbf{R}(n)$, uncorrelated with $\mathbf{w}(n)$. The algorithm is
220 based on two recursive phases, which are briefly described below.

221 *Prediction phase.* Time update, providing *a priori* estimates for the next time step.
 222 The *a priori* state estimate $\hat{\mathbf{x}}(n+1|n)$ is calculated as:

$$\hat{\mathbf{x}}(n+1|n) = \mathbf{A}(n)\hat{\mathbf{x}}(n|n) + \mathbf{B}(n)\mathbf{u}(n), \quad (3)$$

223 and the *a priori* estimate of the state noise covariance $\mathbf{P}(n+1|n)$ is calculated as:

$$\mathbf{P}(n+1|n) = \mathbf{A}(n)\mathbf{P}(n|n)\mathbf{A}^T(n) + \mathbf{Q}(n). \quad (4)$$

224 The time update equations (3) and (4) project forward the state and covariance
 225 estimates from time step n to step $n+1$.

226 *Correction phase.* Measurement update, providing improved *a posteriori* estimates
 227 by incorporating a new measurement. Here n corresponds to what was $n+1$ in the
 228 prediction phase. The optimal Kalman gain $\mathbf{K}(n)$ is firstly calculated as:

$$\mathbf{K}(n) = \mathbf{P}(n|n-1)\mathbf{H}^T(n)[\mathbf{H}(n)\mathbf{P}(n|n-1)\mathbf{H}^T(n) + \mathbf{R}(n)]^{-1}; \quad (5)$$

229 then the *a posteriori* state estimate $\hat{\mathbf{x}}(n|n)$ is calculated as:

$$\hat{\mathbf{x}}(n|n) = \hat{\mathbf{x}}(n|n-1) + \mathbf{K}(n)[\mathbf{z}(n) - \mathbf{H}(n)\hat{\mathbf{x}}(n|n-1)], \quad (6)$$

230 finally, the *a posteriori* estimate of the covariance matrix $\mathbf{P}(n|n)$ is calculated as:

$$\mathbf{P}(n|n) = [\mathbf{I} - \mathbf{K}(n)\mathbf{H}(n)]\mathbf{P}(n|n-1), \quad (7)$$

231 where \mathbf{I} corresponds to the identity matrix. When $n=1$, the initial *a posteriori*
 232 estimate covariance $\mathbf{P}(1|1)$ is set to a determined constant value that represents a
 233 probable error magnitude of the initial estimation. A schematic representation of
 234 the Kalman filter algorithm is depicted in Figure 4.

235 2.2.2. Specific implementation within our block matching framework

236 Our KBM framework involves the integration of a Kalman filtering scheme within
 237 the speckle tracking method, in the objective to cope with the issue of speckle pattern
 238 decorrelation over time, and to avoid tracking errors due to progressive divergence.
 239 Our approach consists in estimating the optimal update of the gray-levels of the
 240 reference block pattern $\mathcal{B}_{ref}(n)$ in each frame of the sequence, prior to the block
 241 matching operation. The rationale of the proposed method is to exploit the cyclic
 242 2D motion of the wall. Indeed, the moving tissues are expected to undergo a small
 243 deformation during the cardiac cycle, which modifies the corresponding speckle pat-
 244 tern, and to periodically recover their original appearance as they return to their

245 initial position. Therefore, our specific update strategy involves the combination of
 246 *i*) a fading memory scheme that takes into account the small deformation of the
 247 moving tissues during the cardiac cycle, and *ii*) a control signal that keeps track of
 248 the initial pattern of the block.

249 Each pixel of the block is considered separately, *i.e.* its state is estimated by an
 250 individual Kalman filter. Indeed, our aim is to avoid the influence between different
 251 regions of the block that may not undergo an identical gray level variation. Without
 252 loss of generality, we describe here the Kalman filtering scheme applied to a single
 253 (*i*-th) pixel of the reference block. In this situation, the vectors \mathbf{x} , \mathbf{z} , $\hat{\mathbf{x}}$, \mathbf{u} , \mathbf{v} and \mathbf{w} ,
 254 as well as the matrices \mathbf{A} , \mathbf{B} , \mathbf{H} , \mathbf{P} , \mathbf{Q} and \mathbf{R} , are reduced to the dimension 1×1 , *i.e.*
 255 scalars. Nevertheless, we keep the vectorial notations. A graphical representation of
 256 our specific Kalman filtering implementation is depicted in Figure 5.

257 The system state $\mathbf{x}(n)$ describes here the gray-level of the same *i*-th pixel at
 258 time n , representing an unknown noise-free value to be estimated. The observa-
 259 tion $\mathbf{z}(n)$ corresponds to the measured noisy gray-level of the pixel at the location
 260 resulting from the previous block matching operation. The estimate $\hat{\mathbf{x}}(n)$ represents
 261 the gray-level of the *i*-th pixel used to construct the reference block.

262 According to our rationale, the control signal \mathbf{u} is defined constant and equal to
 263 the initial gray-level reference $\hat{\mathbf{x}}(1)$ of the *i*-th pixel in $\mathcal{B}_{ref}(1)$. The state transition
 264 matrix \mathbf{A} and the control matrix \mathbf{B} , reduced to scalars, are defined by positive
 265 constants α and β , respectively, such that $\alpha + \beta = 1$. The observation matrix \mathbf{H} is also
 266 defined constant, the corresponding scalar being equal to 1. The observation noise \mathbf{v}
 267 is assumed to correspond to the temporal variations of the gray-level, under the
 268 hypothesis that the tracked speckle pattern should ideally remain constant during the
 269 sequence. In our case, the covariance matrix \mathbf{R} is reduced to a scalar σ_v^2 , calculated
 270 at time step n as the variance of the $(n - 1)$ previously estimated values of $\hat{\mathbf{x}}(n - 1)$,
 271 multiplied by a positive constant scalar γ . When $n = 1$, $\sigma_v^2(1)$ is set to an initial
 272 empirically determined constant value that represents a probable noise magnitude.
 273 Similarly, the covariance matrix \mathbf{P} is reduced to a scalar σ_x^2 and its initial value
 274 has been empirically determined. The process noise \mathbf{w} represents the uncertainty of
 275 the process model and is also assumed to represent a slight variation of the gray-
 276 level. The covariance matrix \mathbf{Q} is reduced to a constant scalar σ_w^2 , the value of which
 277 reflects the magnitude of the expected gray-level variations. This value has also been
 278 empirically determined.

279 Our specific Kalman-based filter is integrated to our KBM algorithm using the
 280 above-detailed parameter settings. At each time step, the reference block $\mathcal{B}_{ref}(n)$ is
 281 thus updated, and then used to seek the position of the best matched block $\mathcal{B}(n + 1)$
 282 within the next image, as depicted in Figure 5. The 2D displacement $\hat{\mathbf{d}}(n + 1)$ between

283 $\mathcal{I}(n)$ and $\mathcal{I}(n + 1)$ is estimated by the block matching framework. To estimate sub-
284 pixel displacements, the reference block and search window are interpolated by a
285 factor 10 during the block matching operation.

286 *2.3. Motion amplitude estimation*

287 Once the 2D trajectory determined, relevant parameters need to be deduced.
288 Previous work suggests that the longitudinal motion amplitude actually is a relevant
289 parameter, *i.e.* it corresponds to a clinical information about vascular health. In our
290 study both longitudinal and radial motion amplitude parameters have been mea-
291 sured from the corresponding trajectory for each subject. The respective amplitudes
292 ΔX and ΔY were calculated as the average value of the peak-to-peak amplitudes
293 measured in two cardiac cycles, for both longitudinal and radial directions (Fig. 6).
294 Such an evaluation of dynamical parameters derived from the trajectory is expected
295 to characterize the potential of our method to provide clinically useful markers.

296 *2.4. Acquisition of in vivo image data*

297 *2.4.1. Study population*

298 Fifty-seven healthy volunteers, as well as 25 patients at high cardiovascular risk
299 and likely to develop atherosclerosis, were involved in this study. The healthy volun-
300 teers were 24 males and 33 females, aged from 19 to 63 years (mean age 37.9 ± 14.1
301 years). The at-risk patients were 16 males and 9 females aged from 34 to 73 years
302 (mean age 56.2 ± 10.5 years). The inclusion criterion for the at-risk patients was the
303 presence of one of the following diseases diagnosed at least 1 year before (Ford, 2005):
304 the metabolic syndrome, or type 1 or 2 diabetes. No other criterion, including clin-
305 ical characteristics, was used to select these subjects. The healthy volunteers were
306 cardiovascular risk factor-free (tobacco use, hypercholesterolemia, diabetes, hyper-
307 tension or particular family history) as assessed by an oral questionnaire. Informed
308 consent was obtained from all participants. The study was conducted in compliance
309 with the requirements of our institutional review board and the ethics committee.

310 *2.4.2. Acquisition of carotid artery ultrasound sequences*

311 Ultrasound acquisition was performed with a medical scanner (Antares, Siemens,
312 Erlangen, Germany), equipped with a 7.5- to 10-MHz linear array transducer. Lon-
313 gitudinal B-mode image sequences of the left CCA were acquired for all subjects.
314 After a 15 minutes rest, the subjects were examined in the supine position with the
315 neck extended and rotated 45° to the contralateral side. The transducer was cen-
316 tered on the CCA, in the longitudinal plane, 2 cm distant from the carotid bulb.
317 The absence of atheromatous plaques in the imaged area was assessed by a medical

318 doctor. Images were recorded through at least two consecutive full cardiac cycles.
319 To avoid the influence of the movement due to breathing, the subjects performed
320 a breath hold during the acquisition. The following instrumentation settings were
321 maintained for all acquisitions: the dynamic range was 65 dB, the sequence frame
322 rate was 26 fps, the pixel size in both radial and longitudinal directions was $30\ \mu\text{m}$.
323 The sequences were stored digitally and transferred to a commercial computer for
324 off-line image analysis. No subject was rejected *a priori* from the study.

325 2.5. Evaluation of the accuracy of our method

326 For each sequence, reference trajectories were generated in the objective to eval-
327 uate the accuracy of our KBM method, despite the lack of ground truth inherent to
328 clinical imaging. Each reference trajectory corresponded to the averaged trajectories
329 resulting from the manual tracings performed by three experienced observers. The
330 inter- and intra-observer variability of these manual tracings was also assessed, one
331 expert performing twice the manual tracking operation for each sequence. More-
332 over, the results of our KBM method were also compared to those obtained with
333 six other state-of-the-art techniques. All resulting 2D trajectories were stored for
334 further analysis.

335 2.5.1. Trajectory reference

336 In the objective to quantify the tracking accuracy of our KBM method, a refer-
337 ence 2D trajectory was constructed over the full length of each sequence. First, a
338 point $\mathbf{p}(1)$ to be tracked, located in the intima-media complex of the carotid distal
339 wall, was selected by the observer O_1 in the first frame of each sequence (Fig. 3).
340 The observer was asked to select a well distinguishable speckle pattern remaining
341 visually perceptible during the whole sequence, in order to make sure that each ob-
342 server will be able to identify the same target all along the sequence. Then, this
343 initial point was tracked over the full length of the sequence, both by the automated
344 KBM processing and by the three observers O_1 , O_2 and O_3 , blinded to the automatic
345 results. For each sequence, the 2D trajectory reference was finally constructed by
346 averaging the results from the three observers, in both radial and longitudinal direc-
347 tions. All resulting 2D trajectories were stored for further analysis. The reference
348 motion amplitude of each sequence was also defined as the peak-to-peak amplitude
349 of the corresponding reference trajectory (Fig. 6). Although we focus in this work
350 on the longitudinal motion amplitude, which corresponds to a risk marker, we also
351 evaluate the radial amplitude. The latter does not represent a clinical information
352 when only estimated on a single wall. Nevertheless, its accuracy also gives an insight
353 to the overall accuracy of the estimated trajectories.

354 *2.5.2. Comparison with other methods*

355 We compared our KBM method with six state-of-the-art tracking methods. We
356 do not pretend to have exactly re-implemented all these methods, which is often
357 not feasible due to the lack of full details in the publications. Instead, we aimed
358 at evaluating the influence of various parameters and concepts. To perform a fair
359 comparison, all the methods considering a single block were initialized with a block
360 centered in the same previously described initial point $\mathbf{p}(1)$, and the methods con-
361 sidering multiple blocks were applied on a region of the wall that included $\mathbf{p}(1)$.

362 *Block matching without Kalman estimator.* A classical BM algorithm (that is to say
363 without Kalman-based update of the reference block) was applied to track the same
364 initial point as our KBM method. To assess the influence of the block and search-
365 window size, three different configuration settings, hereafter denoted as BM, BM_{bis}
366 and BM_{ter} , were used. These respectively correspond to the parameters settings used
367 in *i)* the KBM framework proposed in the present work, *ii)* the echo tracking method
368 proposed in (Cinthio et al., 2005), and *iii)* the block matching method proposed
369 in (Golemati et al., 2003).

370 *Kalman filtering without control signal.* Let us recall that the main feature of our
371 KBM method is the use of a hard memory of the system *via* the control signal \mathbf{u}
372 (Eq. 1), which was not used in the update scheme of the seminal work by Gastouniotti
373 et al. (2011). In order to assess the influence of this signal, we switched it off in our
374 implementation by setting the control matrix to zero ($\beta = 0$). This version, hereafter
375 denoted as KBM_{bis} , was also applied to track the same initial point of each sequence.

376 *Multi-block matching.* All the previously mentioned BM and KBM methods can be
377 classified within the Lagrangian approach, as they all attempt to follow a single target
378 along its trajectory across the spatio-temporal domain. They are all confronted
379 with the problem of speckle decorrelation, which requires a careful design of the
380 update scheme for the reference block. As summarized in Section 1.2.3, the MBM
381 framework (Zahnd et al., 2012) attempts to cope with this problem *via* an Eulerian
382 approach, *i.e.* by estimating the motion at fixed locations within the spatial domain.
383 It involves a contour segmentation scheme aiming to extract the contours of the
384 intima-media complex. At each time step, 16 regularly spaced blocks are repositioned
385 within the intima-media complex, with the upper edge adjacent to the lumen-intima
386 contour. The displacement of each block is estimated independently by seeking the
387 most similar block in the next image, and the resulting displacement of the wall is
388 finally calculated as the median value of all the 16 estimates. In this approach, no
389 memory is used in the update scheme, *i.e.* $\mathcal{B}_{ref}(n) = \mathcal{B}(n)$.

390 *Velocity Vector Imaging.* The VVI commercial software was originally designed to
 391 assess the heart dynamics in US B-mode image sequences. Although it has not
 392 been optimized to assess the arterial wall motion, it was recently used to investigate
 393 the CCA motion (Svedlund et al., 2011; Svedlund and Gan, 2011). We therefore
 394 also compared it with our method, using a similar operating mode. The virtual
 395 transducer used by the software was centered on the top of the screen (Fig. 7a).
 396 The horseshoe-shaped line, originally designed to represent the boundary of the
 397 heart (Fig. 7b), was positioned on the proximal and distal walls with a total of
 398 20 control points. One of its segments was centered on the initial position of the
 399 point $\mathbf{p}(1)$ previously specified by the observer O_1 (Fig. 7a). The 2D motion of the
 400 distal intima-media complex was automatically estimated within the full length of
 401 this segment roughly corresponding to 5 mm. The VVI software displays but does not
 402 export the resulting trajectory (Fig. 7c), so this information was not available for our
 403 study. Only the trajectory amplitudes in the longitudinal (ΔX) and radial (ΔY)
 404 directions, automatically calculated by the VVI software, were stored for further
 405 analysis. We limited this analysis to the healthy volunteers subset, as the results
 406 were relatively poor and the VVI method is relatively labor-consuming and not fully
 407 reproducible, due to the manual placement of the control points. The reproducibility
 408 was assessed by re-running the computation after a new choice of the control points.

409 2.6. Parameter settings

410 Each method was applied on all the sequences with unchanged parameter settings.
 411 These settings are specified below.

412 *Block matching.* The block, search window, and margin dimensions that were used
 413 for our KBM framework as well as the other methods (*i.e.* KBM_{bis} , MBM, BM,
 414 BM_{bis} , and BM_{ter}) are detailed in Table 1. For all methods, the block and window
 415 were systematically interpolated by a factor 10, and the similarity criterion was the
 416 normalized sum of squared differences (NSSD).

417 *Kalman filter.* Our KBM method used the following settings: state-transition matrix
 418 coefficient $\alpha = 0.85$; control matrix coefficient $\beta = 0.15$; initial observation-noise
 419 variance $\sigma_v^2(1) = 25$ (*i.e.* corresponding to a standard deviation of 5 for the gray
 420 level, whose range in the image is $[0, 255]$); process-noise variance $\sigma_w^2 = 25$; initial
 421 estimate variance $\sigma_x^2(1|1) = 25$; covariance matrix coefficient $\gamma = 2$. The KBM_{bis}
 422 method used the same settings except for $\alpha = 1$ and $\beta = 0$.

423 2.7. Statistical analysis

424 The Mann-Whitney U test was used to compare the values of the longitudinal
 425 displacement amplitude ΔX , between healthy volunteers and at-risk patients. The

426 value $p < 0.05$ was considered to indicate a statistically significant difference. All sta-
427 tistical analyses were performed using Intercooled Stata 10.0 (StataCorp LP, College
428 Station, TX, USA).

429 3. Results

430 As previously described, the point \mathbf{p} selected by the observer O_1 within the
431 intima-media complex in the first frame of each sequence, was tracked by the three
432 observers O_1 , O_2 and O_3 , as well as by our KBM method and six other methods
433 (*i.e.* KBM_{bis}, MBM, BM, BM_{bis}, BM_{ter}, and VVI). One sequence, from the healthy
434 group, was excluded *a posteriori* from the evaluation, as the longitudinal trajectories
435 resulting from the observers' tracings were so much different from each other that a
436 reliable reference could not be established. In the remaining 81 sequences, the accu-
437 racy of the methods was evaluated in two ways: by a point-wise comparison of the
438 trajectories and by a global comparison of the resulting amplitudes. The tracking
439 error was defined as the absolute difference between the estimated coordinates of the
440 tracked point and the reference, in each frame of the sequence, for both radial and
441 longitudinal directions. For each trajectory, including the reference, the longitudinal
442 and radial motion amplitudes were calculated by averaging the peak-to-peak ampli-
443 tudes from two different cardiac cycles (Fig. 6). The amplitude estimation error was
444 defined as the difference between the estimated and reference amplitudes, for both
445 radial and longitudinal directions.

446 Before the detailed presentation of the quantitative results, let us show some
447 qualitative examples. The trajectories estimated with our method demonstrated a
448 good similarity with the reference, as depicted in Figure 8. This figure also displays
449 the trajectories resulting from the other methods applied onto the same sequences.
450 To limit the number of curves, instead of the three observers' trajectories, only
451 the reference trajectory and the standard deviation (error bars) introduced by the
452 observers are displayed. In each case, the reference trajectories present a more or less
453 visible "drift", *i.e.* they do not systematically return to their initial position at the
454 end of each cardiac cycle, probably due to a slight contraction of the subject's neck
455 muscles. Nevertheless, the KBM method kept accurate track of the targeted point.
456 In comparison, the other methods generated rather large tracking errors, visible as
457 an increasing divergence (KBM_{bis}, BM), a high jitter (BM_{bis}), or a reduced motion
458 amplitude (MBM, BM_{ter}).

459 As for the processing time, it is proportional to the number of frames in the
460 sequence. The average number of frames in the considered 81 sequences was 116 ± 34
461 (range 66 – 194). Implemented in Matlab (MATLAB 7.13, The MathWorks Inc.,
462 Natick, MA, 2011), our KBM method required, on average, 66 seconds to process
463 the whole sequence, including the interactive initialization, while the manual tracking
464 by the experts took 161 seconds, on average.

465 *3.1. Trajectory estimation*

466 Figure 9 shows a good correlation between the estimated trajectories and the
 467 reference. However, while the estimation of the radial motion component was always
 468 successful ($R = 0.993$), the estimation of the longitudinal component performed
 469 rather poorly for two sequences from the healthy volunteers group, which explains
 470 a weaker correlation ($R = 0.956$). The mean absolute tracking errors, in both lon-
 471 gitudinal and radial directions, for our KBM method and the other methods (*i.e.*
 472 KBM_{bis} , MBM, BM, BM_{bis} and BM_{ter}), are displayed in Table 2. The errors of our
 473 method were of the same order of magnitude as the inter- and intra-observer vari-
 474 ability, whereas the errors generated by the other methods were systematically and
 475 noticeably greater.

476 It is useful to compare the tracking errors with the peak-to-peak amplitude of
 477 the trajectories. The mean values (\pm standard deviation) of the reference longitu-
 478 dinal and radial motion amplitudes in all the 81 assessed subjects were $\overline{\Delta X}_{REF} =$
 479 $634 (\pm 302) \mu\text{m}$ and $\overline{\Delta Y}_{REF} = 373 (\pm 179) \mu\text{m}$, for the longitudinal and radial di-
 480 rections, respectively. More specifically, the reference longitudinal and radial motion
 481 amplitudes were $716 (\pm 275) \mu\text{m}$ and $388 (\pm 198) \mu\text{m}$ for the 56 healthy volunteers, and
 482 $450 (\pm 283) \mu\text{m}$ and $339 (\pm 122) \mu\text{m}$ for the 25 at-risk patients, respectively. Putting
 483 together the ratios between the absolute tracking errors at each time point of each
 484 individual sequence and the longitudinal and radial amplitude of the correspond-
 485 ing individual reference trajectories, the mean values (\pm standard deviation) were:
 486 $15(\pm 20)\%$ of ΔX_{REF} and $7(\pm 9)\%$ of ΔY_{REF} for the 56 healthy volunteers; $20(\pm 20)\%$
 487 of ΔX_{REF} and $7(\pm 9)\%$ of ΔY_{REF} for the 25 at-risk patients; and $16(\pm 20)\%$ of
 488 ΔX_{REF} and $7(\pm 9)\%$ of ΔY_{REF} for all the 81 subjects, respectively.

489 *3.2. Motion amplitude*

490 Table 3 summarizes the errors of the motion amplitudes estimated by our KBM
 491 method, as well as by the other methods (*i.e.* KBM_{bis} , MBM, BM, BM_{bis} , BM_{ter} ,
 492 and VVI), as compared to the reference. The errors of our method were of the same
 493 order of magnitude as the inter- and intra-observer variability, and very close to the
 494 corresponding errors in the position tracking reported in Table 2. Moreover, our
 495 method systematically showed a better accuracy in comparison with all the other
 496 compared methods. Putting together the ratios between the amplitude errors gener-
 497 ated on each individual sequence and the amplitude of the corresponding individual
 498 reference trajectory, the mean values (\pm standard deviation) were: $12(\pm 11)\%$ of
 499 ΔX_{REF} and $6(\pm 7)\%$ of ΔY_{REF} for the 56 healthy volunteers; $14(\pm 11)\%$ of ΔX_{REF}
 500 and $6(\pm 5)\%$ of ΔY_{REF} for the 25 at-risk patients; and $13(\pm 11)\%$ of ΔX_{REF} and
 501 $6(\pm 7)\%$ of ΔY_{REF} for all the 81 subjects.

502 Figure 10 shows a good correlation between the estimated amplitudes and the
503 reference. For the already mentioned reasons (loss of the longitudinal track in two
504 sequences), the correlation was better in the radial direction ($R=0.992$) than in the
505 longitudinal direction ($R=0.952$). The Bland and Altman plots (Fig. 11) demon-
506 strate an overall good agreement of the amplitudes between our method and the
507 reference, with the 95% confidence intervals of $189\ \mu\text{m}$ (30% of $\overline{\Delta X}_{REF}$) and $46\ \mu\text{m}$
508 (12% of $\overline{\Delta Y}_{REF}$) for the longitudinal and radial direction, respectively. Figure 11
509 also shows that, on average, the estimated amplitudes were slightly under-evaluated
510 in comparison to the reference: $-31\ \mu\text{m}$ and $-6\ \mu\text{m}$ in the longitudinal and radial
511 directions. This under-evaluation was not larger than the pixel size and small in com-
512 parison with the corresponding amplitudes: -5% of $\overline{\Delta X}_{REF}$ and -2% of $\overline{\Delta Y}_{REF}$,
513 respectively.

514 The dispersion of the estimated motion amplitude, for our KBM method, the six
515 other methods (*i.e.* KBM_{bis} , MBM, BM, BM_{bis} , BM_{ter} , and VVI), and the three
516 observers, is displayed in Figure 12 (please remind that the VVI software was only
517 applied on the sequences from the 56 healthy volunteers). The boxes and error bars
518 representing the distribution of the errors w.r.t. the reference are tighter for the
519 observers than for our KBM method, which is quite normal, as the reference was
520 built up based on the observers' tracings. Nevertheless, the boxes and error bars
521 for our KBM method remain relatively narrow and close to those for the observers,
522 while the distribution of the errors resulting from the other methods shows a greater
523 dispersion with a larger average under-evaluation of the longitudinal and radial di-
524 rections amplitudes: $-106\ \mu\text{m}$ and $-15\ \mu\text{m}$ for KBM_{bis} ; $-215\ \mu\text{m}$ and $-29\ \mu\text{m}$ for
525 MBM; $-162\ \mu\text{m}$ and $-41\ \mu\text{m}$ for BM; $-60\ \mu\text{m}$ and $-15\ \mu\text{m}$ for BM_{bis} ; $-335\ \mu\text{m}$ and
526 $-76\ \mu\text{m}$ for BM_{ter} ; $-244\ \mu\text{m}$ and $-83\ \mu\text{m}$ for VVI.

527 3.2.1. Statistical analysis

528 The result of the Mann-Whitney U test demonstrated that the peak-to-peak
529 amplitude of the longitudinal motion ΔX , estimated with our KBM method, was
530 significantly reduced in at-risk patients compared to healthy volunteers ($408 \pm 281\ \mu\text{m}$
531 *vs* $643 \pm 274\ \mu\text{m}$, $p < 0.0001$, Fig. 13).

532 Let us note that the peak-to-peak amplitude of the radial motion ΔY does not
533 correspond to the cross-sectional diameter change, as the motion of only one wall
534 was assessed, therefore no statistical comparison of this parameter between the two
535 groups was realized.

536 4. Discussion and Conclusion

537 4.1. On the proposed method

538 To estimate the 2D motion of the arterial tissues, we introduced a novel block
539 matching method that involves a specific Kalman filtering scheme. The Kalman
540 filter is used to optimally update the gray levels of the reference block containing the
541 tracked pattern. This update strategy is performed pixel-wise, *i.e.* each pixel of the
542 reference block is considered independently, in order to avoid the influence between
543 different parts of the block that may not follow the same gray-level variation. By
544 using the initial pattern appearance as control signal, we have successfully addressed
545 the problem of speckle decorrelation inherent to US imaging of moving tissues: the
546 reference block appearance evolves to take into account the observed variations, but
547 this evolution does not lead to divergence.

548 Similarly to the previously published work, we have chosen to estimate one single
549 trajectory that is expected to characterize the stiffness of the whole arterial wall
550 section. To this purpose, we recommend to select a single salient echo, which enables
551 the user to visually check the correctness of the tracking result and probably makes
552 the tracking more robust. Although the at-risk patients are often less echogenic
553 than the healthy subjects, such a well-distinguishable echo scatterer was perceptible
554 through the entire sequence in all but one out of the 82 subjects involved in our
555 evaluation. Nevertheless, despite its overall best performance, our method poorly
556 estimated the longitudinal motion in two sequences from the healthy group. There-
557 fore, we recommend to systematically perform a visual inspection, once the process
558 is over, to check whether: *i*) the resulting 2D trajectory is cyclic and reproducible,
559 and *ii*) the estimated block location is always superimposed onto the pattern of in-
560 terest. These checking operations can be performed very easily and quickly thanks
561 to a smart implementation, allowing the user to display the results.

562 As the use of a salient point was mandatory to perform reliable manual track-
563 ing and build the reference trajectories, we did not investigate the variability of the
564 estimated wall motion when varying the initial point to be tracked. Moreover, our
565 experience suggests that different sections of the wall actually undergo slightly dif-
566 ferent displacements. A thorough investigation of this phenomenon was beyond the
567 scope of this article, as well as the assessment of the method's sensitivity to varying
568 imaging parameters (*i.e.* gain, central frequency, frame rate, or pixel size).

569 In our study, the sequences were acquired with the same ultrasound scanner and
570 by the same medical doctor. We expect that some parameters of the algorithm have
571 to be adjusted if the image acquisition settings change. Namely, the Kalman model
572 provides optimal results if the covariance matrices \mathbf{P} , \mathbf{Q} and \mathbf{R} (*cf* Section 2.2.2)

573 correctly reflect the noise levels of the system. The corresponding variances σ_x^2 ,
574 σ_w^2 and σ_v^2 have been empirically determined (*cf* Section 2.6), based on sequences
575 acquired in the same conditions (*cf* Section 2.4.2), and are likely not to be optimal
576 if the actual gain and noise levels change significantly. Similarly, the block \mathcal{B} has to
577 encompass the tracked salient echo scatterer (Fig. 3). Its size was set empirically in
578 our study and may require modifications depending on the spatial definition of the
579 actual ultrasound scanner. One limitation of our method is related to the assumption
580 that the tracked pattern periodically recovers its initial appearance and location.
581 This assumption holds if the ultrasonographer is experienced enough to hold the
582 probe immobile with respect to the carotid artery.

583 4.2. On the compared methods

584 The previously published work mainly differs from our method in two aspects:
585 block/window size and update strategy.

586 Concerning the update strategy, we compared four approaches, using the same
587 block size. Three of them, namely KBM, KBM_{bis} and BM, perform a Lagrangian
588 tracking of a single block, whereas the fourth one, MBM (Zahnd et al., 2012), rather
589 falls into the Eulerian motion-estimation category and uses multiple blocks. Our
590 KBM method performed the best, while KBM_{bis} was ranked second, due to a pro-
591 gressive divergence in the trajectory estimation (Fig. 8). As the latter method uses
592 a Kalman filtering scheme without control signal \mathbf{u} , similarly to (Gastouniotti et al.,
593 2011), this result illustrates how important it is to integrate the initial pattern $\mathcal{B}_{ref}(1)$
594 in the update strategy of the reference block. The classical BM method, without
595 Kalman filter, generated larger errors and showed an increased divergence (Fig. 8),
596 caused by cumulating the successive errors due to the “hard” update (*i.e.* using
597 the block found in the previous frame as reference). Despite the use of the same
598 “hard” update, MBM performed almost as well as KBM_{bis} from the tracking ac-
599 curacy point of view. This is probably a beneficial combination of two effects: *i*)
600 longitudinal block repositioning at fixed grid locations, according to the Eulerian
601 approach, which partly avoids cumulating the successive errors, and *ii*) the use of
602 multiple blocks, which partly compensates the incorrect estimates. However, the
603 counterpart of combining the estimates from multiple blocks is that large displace-
604 ments are discarded and the motion amplitude is thus significantly underestimated.

605 As for the block size, in our KBM method we have chosen to adapt its width
606 (1.50 mm) to the typical width of salient echo scatterers and its height (0.30 mm)
607 to the thickness of the intima-media complex (the latter in the objective to avoid
608 the inclusion of neighboring differently moving tissues). The same size was used
609 by the BM method and compared to the variants using the same update strategy

610 with a smaller or larger block size: BM_{bis} and BM_{ter} , respectively. The largest
611 tracking errors were obtained with reduced block and window dimensions (BM_{bis}),
612 as proposed in (Cinthio et al., 2005). Several mismatches can be observed as a
613 jitter in the trajectory (Fig. 8). Cinthio et al. (2005) have previously reported very
614 accurate results, but the images were acquired on a different scanner, with a very
615 careful protocol, which resulted in a better quality. We therefore suggest that such
616 a small block size leads to a high noise-sensitivity and is not well suited to current
617 clinically acquired sequences. Conversely, a large block/window size (BM_{ter}), such
618 as the one used by Golemati et al. (2003), is more robust to noise, but the estimated
619 trajectory does not achieve the entire motion amplitude. Additional errors are due
620 to the fact that the block encompasses several differently moving regions.

621 It is interesting to remark that comparable tracking errors (*e.g.* KBM_{bis} vs MBM
622 or BM vs BM_{ter}) do not necessarily imply similar amplitude errors, and *vice-versa*.
623 We have observed that a method that diverges (*i.e.* progressively tracks a pattern
624 different than the initial one), may nevertheless reasonably well capture the motion
625 amplitude (Fig. 8). This mainly happens for the methods that use a reduced spatio-
626 temporal support, such as KBM_{bis} and BM . Conversely, a method that provides
627 stable trajectories, thus generating relatively small tracking errors, may fail to cap-
628 ture the full dynamics of the motion. Such under-evaluation of the motion amplitude
629 rather occurs with methods using a larger spatial support, such as MBM and BM_{ter} .

630 We also included in our evaluation the VVI method that was recently used to
631 study the longitudinal motion of the arterial wall in carotids (Svedlund and Gan,
632 2011; Svedlund et al., 2011), although its principle can hardly be compared with
633 block-matching methods. However, it ranked penultimate, which can be explained
634 by the fact that the VVI commercial software was not optimized for this application
635 and also by the use of a relatively large spatial support.

636 As expected, both motion tracking and amplitude estimation errors generated
637 by all methods, including KBM, were greater in the longitudinal direction compared
638 to the radial direction. This is caused by the previously mentioned two factors
639 that contribute to make challenging the assessment of the longitudinal arterial-wall
640 motion in *in vivo* US images: *i*) lack of acoustic interfaces in this direction, and *ii*)
641 shape of the US-scanner PSF.

642 4.3. On the clinical applications

643 As the longitudinal motion has been evidenced recently (Persson et al., 2003),
644 relatively few (semi)automatic methods have been proposed to investigate clinically
645 this phenomenon. Nevertheless, although they were less accurate and/or more noise-
646 sensitive than our method, the published studies have demonstrated that the longitu-

647 dinal motion amplitude can provide relevant and complementary information about
648 arterial physiopathology. In particular, according to Svedlund et al. (2011) the longi-
649 tudinal motion amplitude can predict 1-year cardiovascular outcome independently
650 of other risk factors. It has also been shown that this parameter undergoes profound
651 changes in response to catecholamines (Ahlgren et al., 2009, 2012). The authors
652 have deduced from this finding that the mental stress, which is considered as a risk
653 factor for the cardiovascular disease, is correlated with the endothelial shear strain
654 (calculated using the longitudinal motion amplitudes at the inner and outer bound-
655 aries of the intima-media complex). Based on three clinical studies, our team has
656 shown that the amplitude of the longitudinal motion does not simply replicate the
657 information provided by traditional risk markers, but is rather likely to represent a
658 complementary marker of early arterial wall abnormalities. In the first study (Zahnd
659 et al., 2011a), young healthy volunteers were compared to elderly diabetic patients.
660 This proof of concept confirmed that the longitudinal motion amplitude was sig-
661 nificantly reduced in at-risk patients compared to healthy controls. In the second
662 study (Zahnd et al., 2011b), three populations were compared: young healthy sub-
663 jects, elderly healthy subjects and elderly diabetic patients, using the shear index
664 (a parameter based on the longitudinal motion amplitudes) and the distensibility
665 (conventional marker based on the radial motion). When using the former, a signif-
666 icant difference has been found between both healthy populations and the diabetic
667 patients, but not between young and elderly healthy volunteers. When using the
668 latter, a significant difference has been found between the young healthy volunteers
669 and both elderly populations, but not between the diabetic patients and the elderly
670 healthy volunteers. In the third study (Zahnd et al., 2012), patients with periodontal
671 disease were compared to a control group of the same age, using the shear index and
672 the distensibility. The former evidenced a significant difference between the patients
673 and the control group, while no significant difference was found when using the latter
674 parameter.

675 The goal of this article was to present our KBM method and to evaluate its
676 accuracy, but neither to tackle a specific new clinical problem, nor to assess the
677 relevance of the longitudinal motion as compared to traditional cardiovascular risk
678 markers. Patients at high cardiovascular risk were included in the study because they
679 are often less echogenic, which leads to a decreased image quality. A “side effect” was
680 to confirm that the longitudinal motion amplitude, estimated using this method, was
681 significantly reduced in at-risk patients compared to healthy volunteers. Now that
682 the KBM method has demonstrated its accuracy, it can be used to investigate the
683 arterial wall motion more thoroughly. In particular, beyond the motion amplitude, it
684 can be interesting to explore parameters characterizing the shape of the trajectories.

685 More generally, the cause of wall longitudinal motion still remains to be con-
686 firmed. We suggest that blood friction, creating a tangential force at the surface of
687 the wall, only constitutes a minor contribution. Indeed, we propose that the ante-
688 grade wall longitudinal motion may rather be coupled to the radial systolic stretching
689 caused by the blood volume influx (this phenomenon being different to the propa-
690 gation of the pulse wave, generated by the systolic stroke volume). We also suggest
691 that the retrograde wall longitudinal motion is induced by a first protosystolic back-
692 ward motion caused by the apical motion of the aortic valve annulus, and a second
693 mesosystolic backward motion caused by the reflected wave. Future applications of
694 our KBM method may contribute to a better understanding of this phenomenon.

695 4.4. Conclusion

696 The longitudinal motion of the arterial wall, which remains a challenging pa-
697 rameter to assess with accuracy, is likely to constitute a novel complementary and
698 relevant clinical information about vascular health. To address this problematic and
699 investigate this phenomenon, we have presented a method to assess *in vivo* the 2D
700 motion of the arterial wall, and evaluated it on the distal wall of 82 US B-mode
701 sequences of human CCA. Our method involves a Kalman-based block matching
702 framework, requires minimal user interaction, and provides results of the same order
703 of accuracy as those manually obtained by experienced observers, while remaining
704 much faster and fully reproducible. The proposed method can already constitute a
705 reliable technique to investigate vascular health in clinical studies.

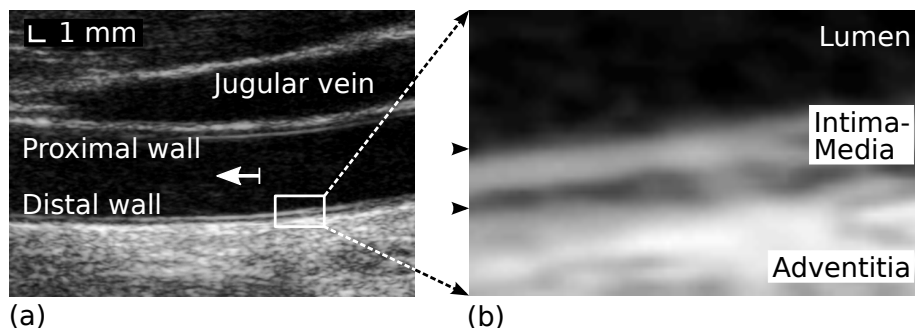


Figure 1: Structure of the CCA. (a) Ultrasound B-mode image of a longitudinal section. The blood direction is indicated by the white arrow. (b) Detailed region of the distal wall, showing the lumen and the three tissue layers. The location of the lumen-intima and the media-adventitia interfaces is displayed by the two black triangles.

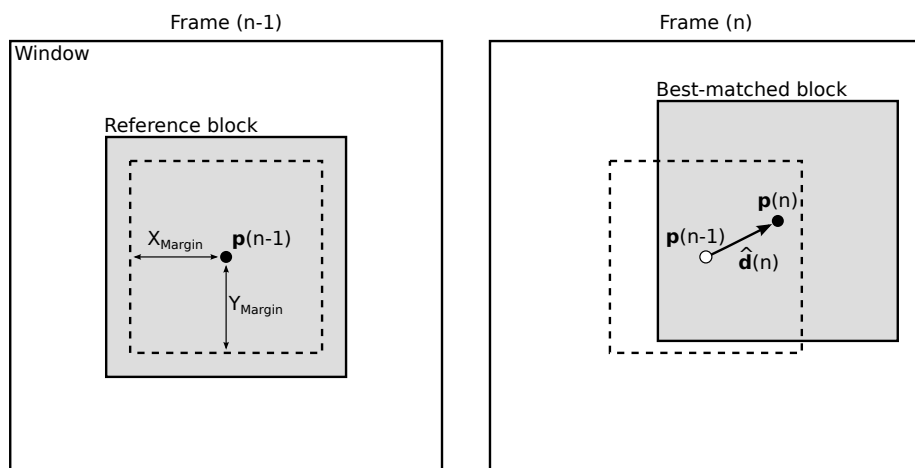


Figure 2: Block matching schematic diagram. The displacement $\hat{\mathbf{d}}(n)$ corresponds to the motion from the reference block centered on the point $\mathbf{p}(n-1)$ to the location of the best matched block centered on the point $\mathbf{p}(n)$ between the $(n-1)^{\text{st}}$ and the n^{th} frames. The search window corresponds to the whole investigated neighborhood defined by the maximal displacement margins $[X_{Margin}, Y_{Margin}]$, delimited by the dashed square.

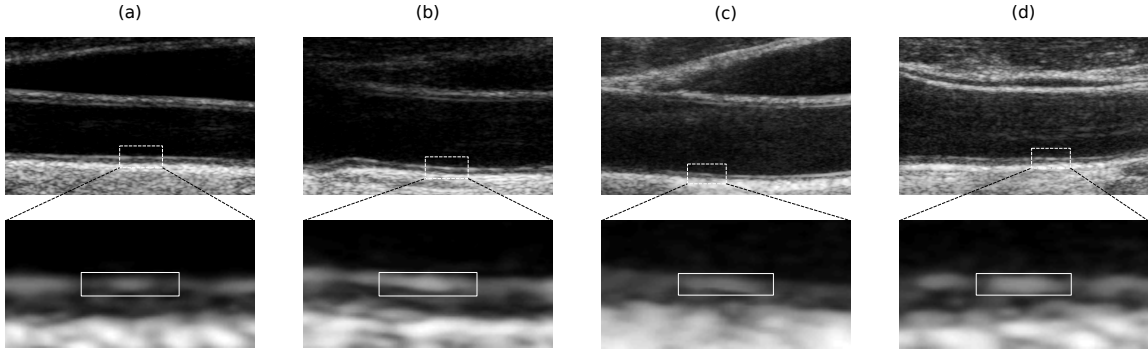


Figure 3: Example of US B-mode images of the CCA, from two healthy volunteers (a, b) and two at-risk patients (c, d). For each subject, the enlarged region (bottom) corresponds to the white dashed rectangle (top). Within the intima-media complex of the distal wall, the block \mathcal{B} (white solid rectangle, $1.50 \times 0.30 \text{ mm}^2$) is centered on the tracked point \mathbf{p} , *i.e.* an echo scatterer generating a well-distinguishable speckle pattern.

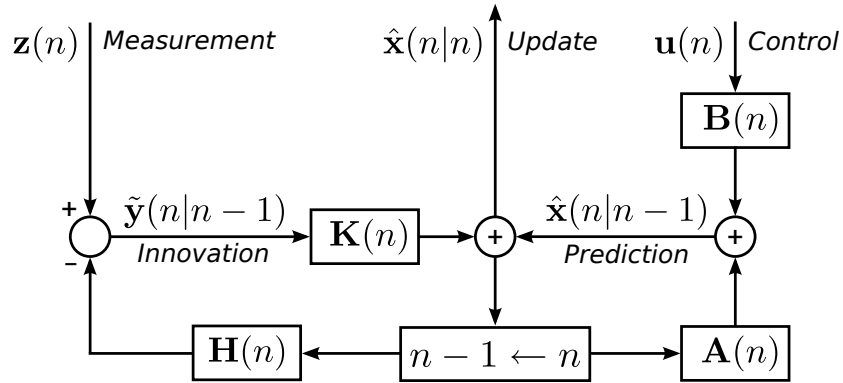


Figure 4: Schematic representation of the Kalman filter algorithm. In our context, the measurement $\mathbf{z}(n)$ corresponds to the current best-matched block $\mathcal{B}(n)$, the control signal $\mathbf{u}(n)$ corresponds to the initial reference block $\mathcal{B}_{ref}(1)$, and the update $\hat{\mathbf{x}}(n|n)$ corresponds to the reference block $\mathcal{B}_{ref}(n)$.

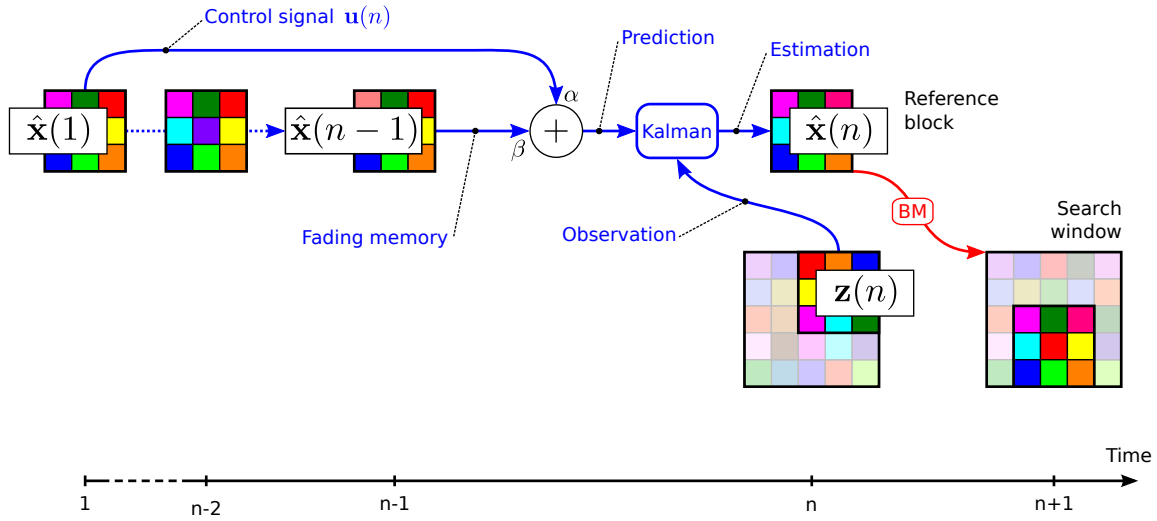


Figure 5: Illustration of our specific Kalman Block Matching (KBM) method. The Kalman filter is used pixel-wise to estimate the gray level $\hat{\mathbf{x}}(n)$ of the reference block $\mathcal{B}_{ref}(n)$, given the previous estimation $\hat{\mathbf{x}}(n-1)$, the control signal $\mathbf{u}(n)$ (i.e. the initial reference block $\mathcal{B}_{ref}(1)$), and the observation $\mathbf{z}(n)$ (i.e. the best-matched block $\mathcal{B}(n)$). A block matching (BM) operation is finally carried out to estimate the displacement between the two considered subsequent frames, using the estimated reference block.

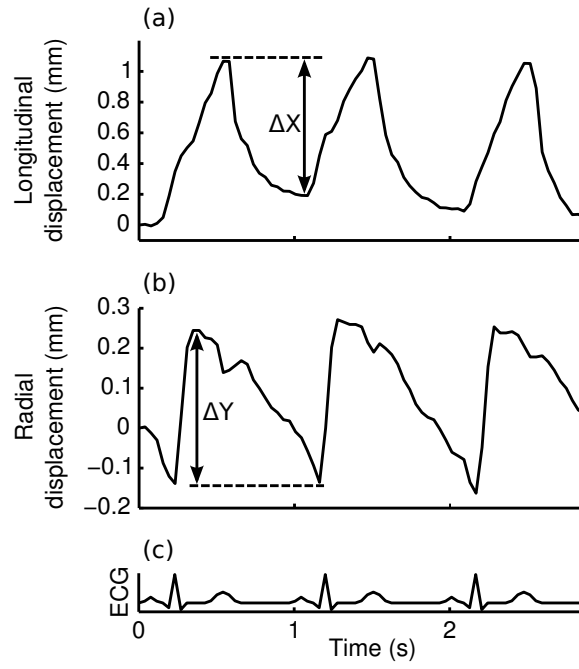


Figure 6: Example of trajectories and respective amplitudes: ΔX , in the longitudinal direction (a), and ΔY in the radial direction (b), with the corresponding ECG (c).

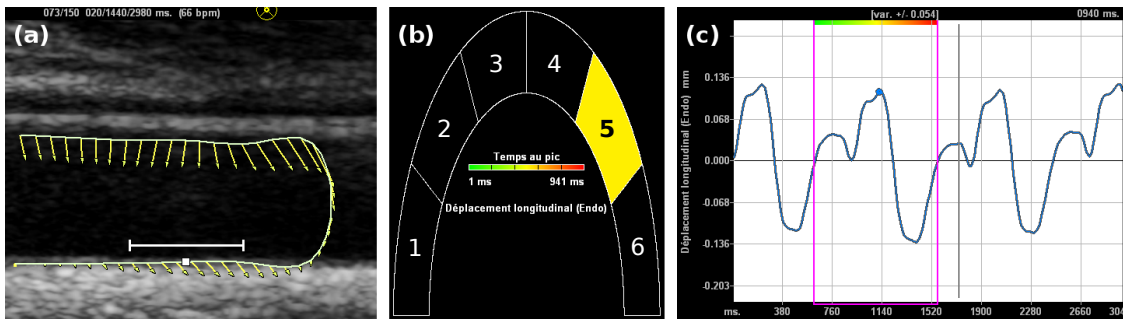


Figure 7: Velocity Vector Imaging (VVI) commercial software. (a) Longitudinal view of the carotid artery, with the position of the tracked point p previously selected by the observer O_1 (white square). The horseshoe-shaped set of control points is positioned in order to center the tracked point p in the middle of the segment identified by a white bar and corresponding to the fifth zone (yellow) in (b). (b) Representation of the six zones defining the horseshoe-shape, where the 5th one (yellow) corresponds to the white bar in (a). (c) Resulting longitudinal trajectory of the region corresponding to the 5th segment.

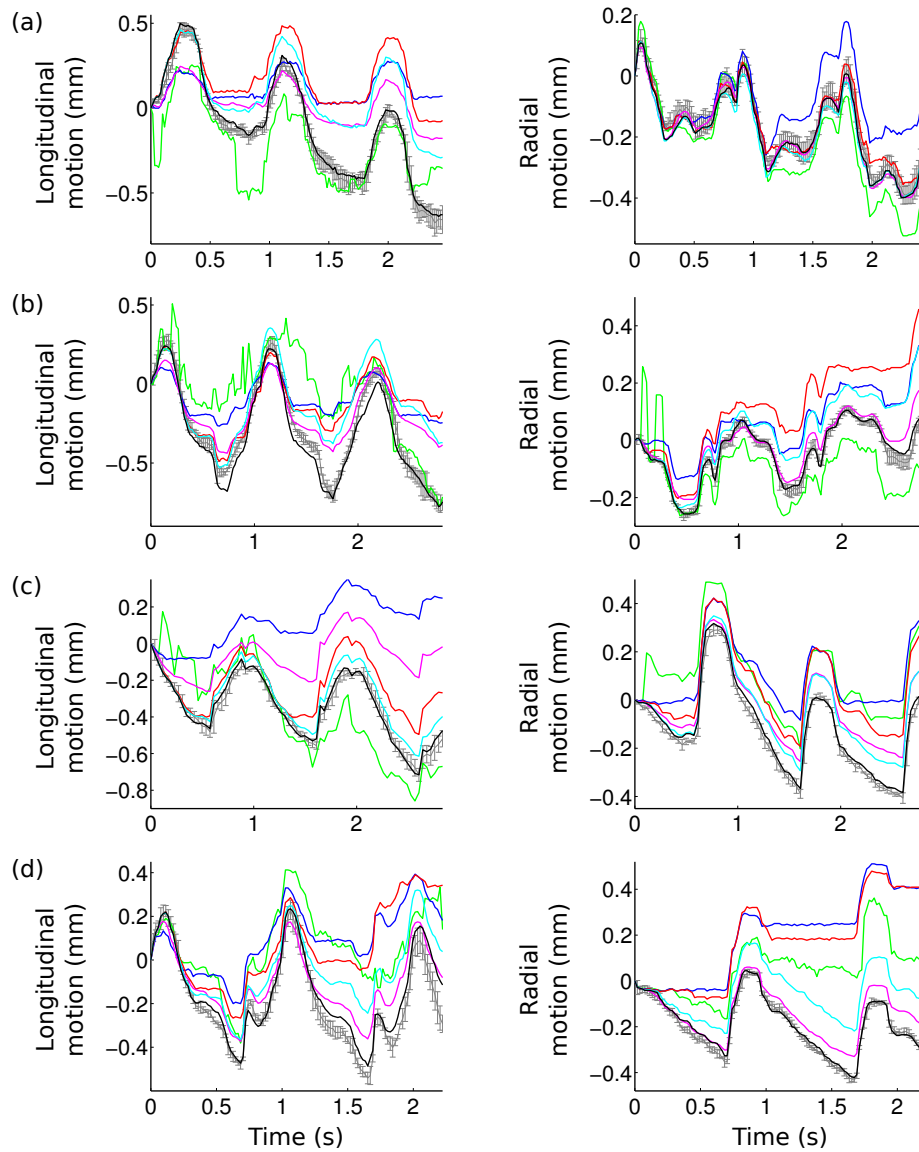


Figure 8: Results of the trajectory estimation over several cardiac cycles, from two healthy volunteers (a, b) and two at-risk patients (c, d), in the longitudinal (left) and radial (right) directions, for our KBM method (black), as well as for KBM_{bis} (cyan), MBM (magenta), BM (red), BM_{bis} (green), and BM_{ter} (blue). The reference trajectory (gray) is displayed together error bars representing the variability (standard deviation) introduced by the three observers O_1 , O_2 and O_3 .

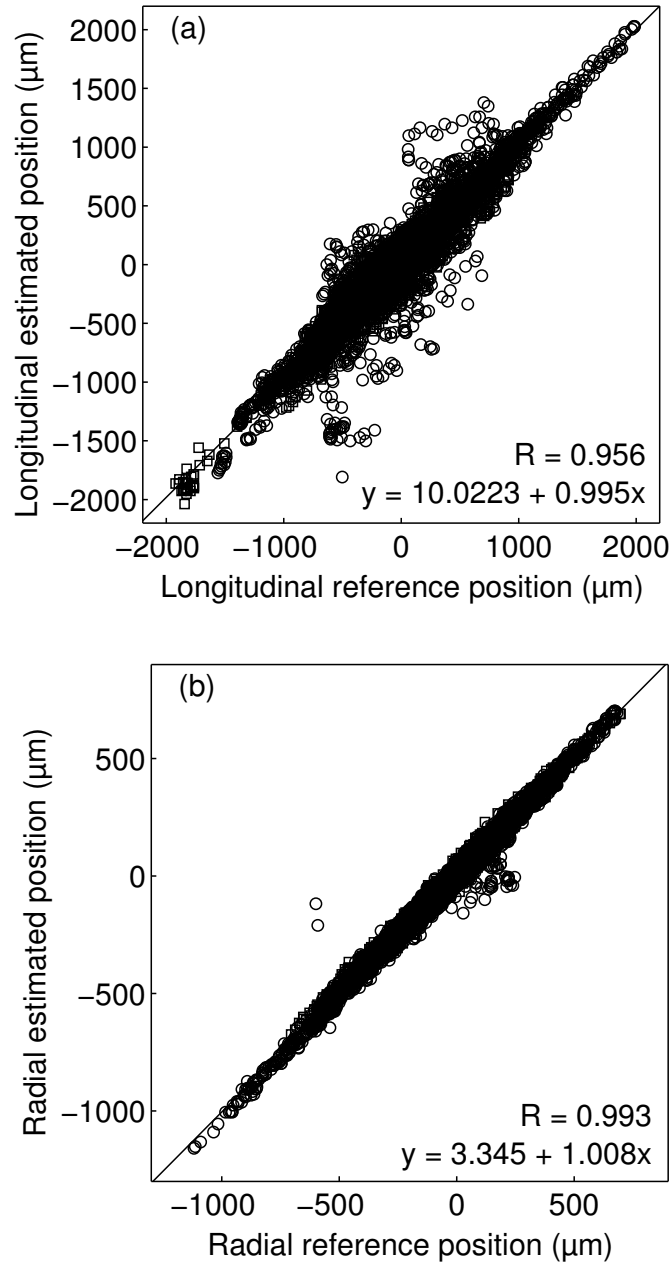


Figure 9: Linear regression line and correlation coefficient R between the reference position of the tracked point \mathbf{p} and its estimation performed by our KBM method, during the whole length of each sequence, for healthy volunteers (circles) and at-risk patients (squares), in the longitudinal (a) and radial (b) directions. For each sequence, the zero coordinate corresponds to the position of the point in the first frame.

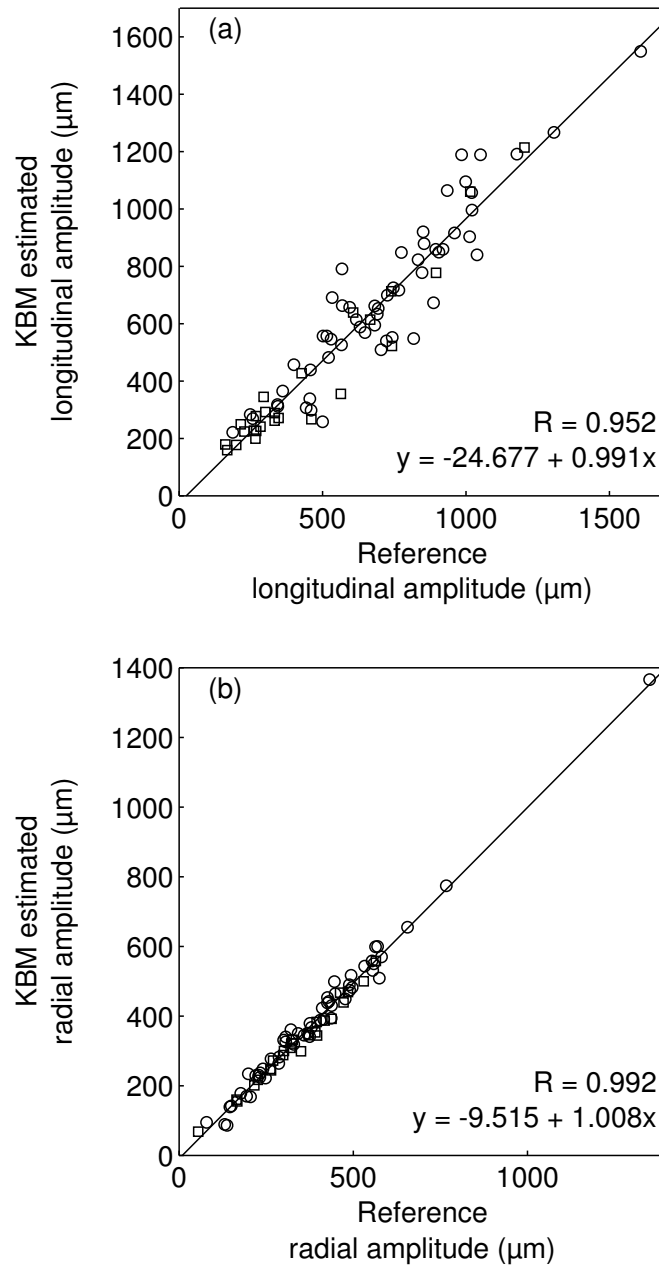


Figure 10: Linear regression line and correlation coefficient R between the reference value of the motion amplitude and the estimation performed by our KBM method, for healthy volunteers (circles) and at-risk patients (squares), in the longitudinal (ΔX , a) and radial (ΔY , b) directions.

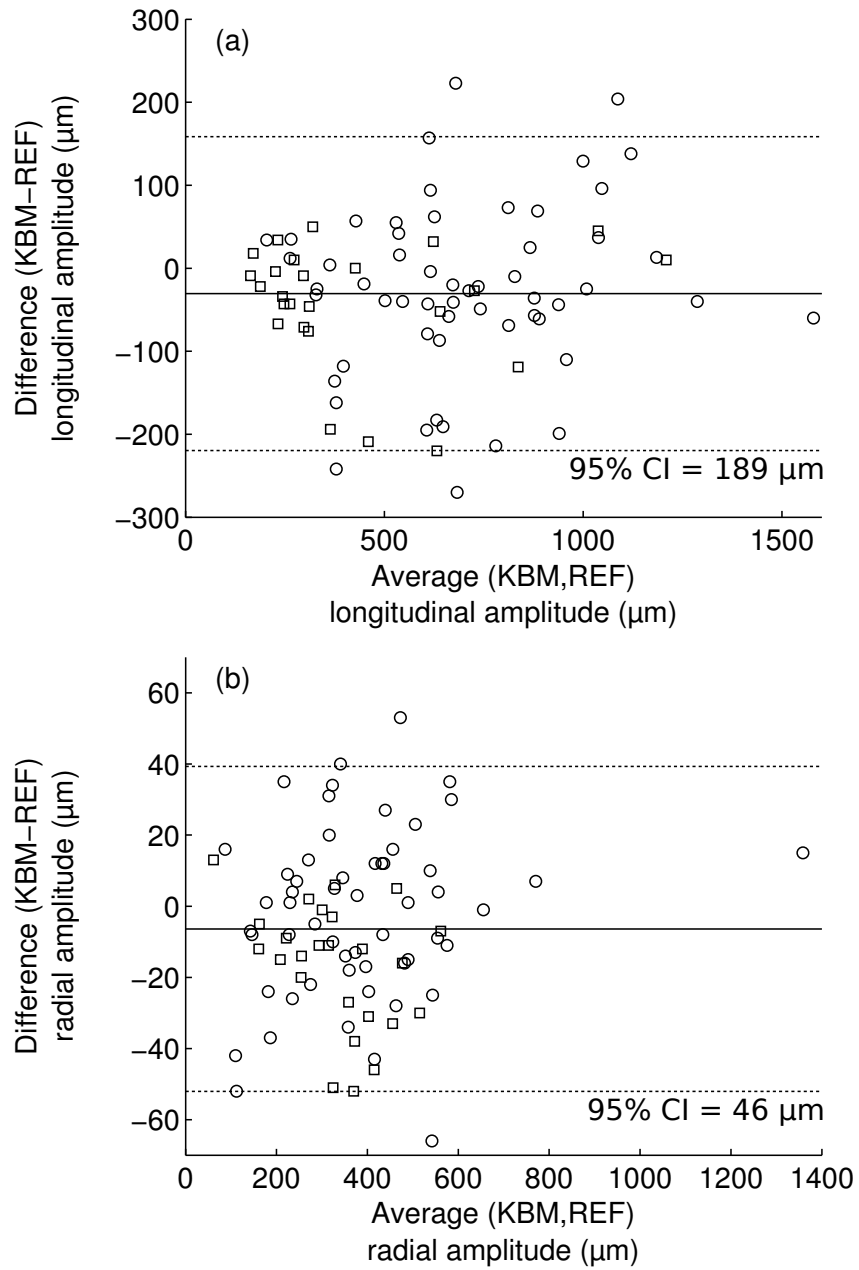


Figure 11: Bland-Altman plot comparing the motion amplitude estimated by our KBM method with the reference (REF), for healthy volunteers (circles) and at-risk patients (squares), in the longitudinal (ΔX , a) and radial (ΔY , b) direction.

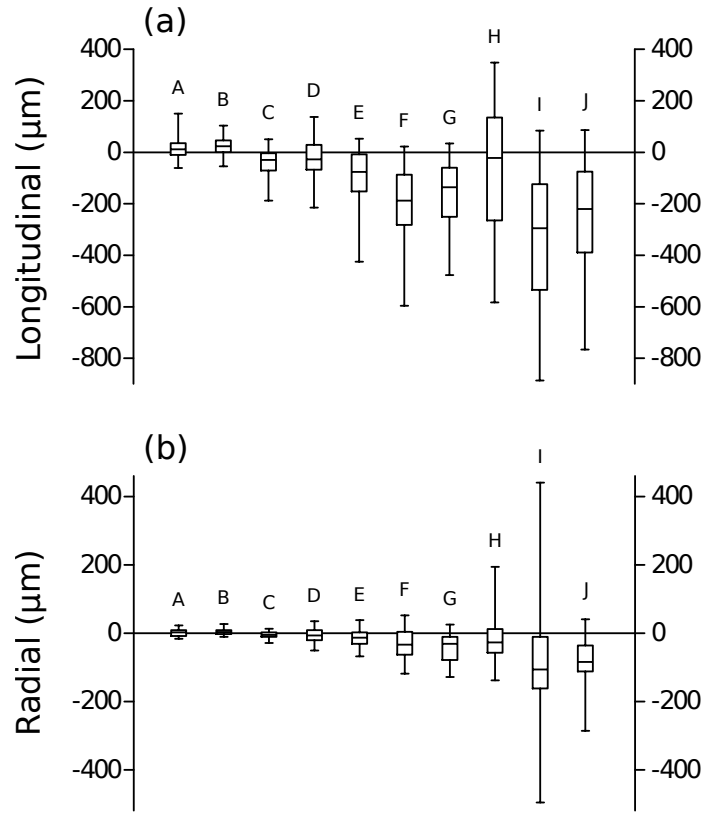


Figure 12: Box plot representing the dispersion of the estimated motion amplitude from the reference (zero level), in the longitudinal (ΔX , a) and radial (ΔY , b) directions, for the three observers O_1 , O_2 , and O_3 (A-C), KBM (D), KBM_{bis} (E), MBM (F), BM (G), BM_{bis} (H), BM_{ter} (I), and VVI (J). Percentiles are indicated by boxes (25th and 75th), inner lines (50th) and error bars (5th and 95th).

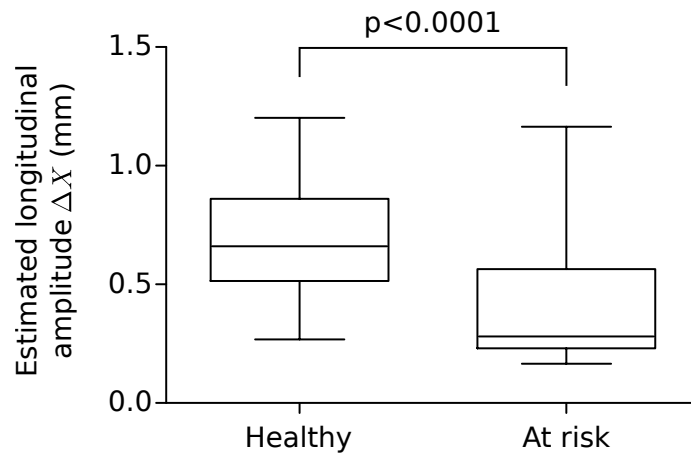


Figure 13: Box plot representing the longitudinal motion amplitude, for healthy volunteers and at-risk patients. Percentiles are indicated by boxes (25th and 75th), inner lines (50th) and error bars (5th and 95th). The result of the Mann–Whitney U test is indicated by the p value.

Table 1: Parameter settings for the different block matching methods

Method	Size: longitudinal \times radial		
	Block	Window	Margin
KBM, KBM _{<i>bis</i>} , BM	$1.50 \times 0.30 \text{ mm}^2$	$2.50 \times 1.30 \text{ mm}^2$	$[0.50, 0.50] \text{ mm}$
MBM	$1.50 \times 0.30 \text{ mm}^2$	$2.50 \times 0.70 \text{ mm}^2$	$[0.50, 0.20] \text{ mm}$
BM _{<i>bis</i>}	$0.10 \times 0.10 \text{ mm}^2$	$0.70 \times 0.70 \text{ mm}^2$	$[0.30, 0.30] \text{ mm}$
BM _{<i>ter</i>}	$3.20 \times 2.50 \text{ mm}^2$	$4.50 \times 3.80 \text{ mm}^2$	$[0.65, 0.65] \text{ mm}$

Table 2: Tracking absolute errors in μm

Method	Longitudinal	Radial
Healthy (n=56)		
KBM <i>vs</i> Reference	89 ± 117	20 ± 20
KBM _{<i>bis</i>} <i>vs</i> Reference	170 ± 185	58 ± 62
BM <i>vs</i> Reference	235 ± 239	111 ± 111
BM _{<i>bis</i>} <i>vs</i> Reference	592 ± 569	194 ± 304
BM _{<i>ter</i>} <i>vs</i> Reference	223 ± 202	102 ± 113
MBM <i>vs</i> Reference	174 ± 177	46 ± 49
Inter-observers variability	97 ± 142	25 ± 30
Intra-observer variability	71 ± 125	15 ± 19
At-risk (n=25)		
KBM <i>vs</i> Reference	69 ± 72	20 ± 16
KBM _{<i>bis</i>} <i>vs</i> Reference	111 ± 146	63 ± 52
BM <i>vs</i> Reference	160 ± 156	142 ± 129
BM _{<i>bis</i>} <i>vs</i> Reference	307 ± 278	195 ± 272
BM _{<i>ter</i>} <i>vs</i> Reference	175 ± 152	124 ± 121
MBM <i>vs</i> Reference	125 ± 115	42 ± 35
Inter-observers variability	59 ± 51	23 ± 20
Intra-observer variability	32 ± 26	10 ± 8
All (n=81)		
KBM <i>vs</i> Reference	84 ± 107	20 ± 19
KBM _{<i>bis</i>} <i>vs</i> Reference	154 ± 177	59 ± 60
BM <i>vs</i> Reference	215 ± 222	120 ± 117
BM _{<i>bis</i>} <i>vs</i> Reference	515 ± 523	194 ± 296
BM _{<i>ter</i>} <i>vs</i> Reference	210 ± 191	108 ± 116
MBM <i>vs</i> Reference	161 ± 164	45 ± 45
Inter-observers variability	87 ± 125	24 ± 28
Intra-observer variability	60 ± 109	13 ± 17

Table 3: Peak-to-peak amplitude absolute errors in μm

Method	Longitudinal	Radial
Healthy (n=56)		
KBM <i>vs</i> Reference	82 ± 70	19 ± 15
KBM _{<i>bis</i>} <i>vs</i> Reference	141 ± 134	26 ± 22
BM <i>vs</i> Reference	208 ± 146	47 ± 39
BM _{<i>bis</i>} <i>vs</i> Reference	249 ± 219	64 ± 76
BM _{<i>ter</i>} <i>vs</i> Reference	391 ± 213	79 ± 41
MBM <i>vs</i> Reference	262 ± 183	53 ± 41
VVI <i>vs</i> Reference	263 ± 207	95 ± 76
VVI variability	128 ± 117	40 ± 48
Inter-observers variability	95 ± 118	16 ± 17
Intra-observers variability	79 ± 119	21 ± 22
At risk (n=25)		
KBM <i>vs</i> Reference	58 ± 63	19 ± 15
KBM _{<i>bis</i>} <i>vs</i> Reference	69 ± 88	22 ± 20
BM <i>vs</i> Reference	116 ± 121	53 ± 48
BM _{<i>bis</i>} <i>vs</i> Reference	179 ± 109	67 ± 73
BM _{<i>ter</i>} <i>vs</i> Reference	194 ± 144	100 ± 54
MBM <i>vs</i> Reference	130 ± 132	41 ± 30
Inter-observers variability	43 ± 34	17 ± 15
Intra-observer variability	25 ± 25	8 ± 7
All (n=81)		
KBM <i>vs</i> Reference	74 ± 68	19 ± 15
KBM _{<i>bis</i>} <i>vs</i> Reference	118 ± 125	25 ± 21
BM <i>vs</i> Reference	180 ± 144	49 ± 42
BM _{<i>bis</i>} <i>vs</i> Reference	228 ± 194	65 ± 75
BM _{<i>ter</i>} <i>vs</i> Reference	330 ± 212	85 ± 46
MBM <i>vs</i> Reference	221 ± 179	49 ± 38
Inter-observers variability	79 ± 103	16 ± 16
Intra-observer variability	62 ± 103	17 ± 19

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