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Tracking and Monitoring Pulsatility of a Portion of Inferior Vena Cava from Ultrasound Imaging in Long Axis

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Abstract

Pulsatility of the inferior vena cava (IVC) provides information on the volume status in healthy subjects and in many clinical conditions. The ultrasound (US) approach to estimate the caval index (CI) is not standardized, as it is operator-dependent and prone to measurement errors due to different factors, including movements of the IVC and non-uniform IVC pulsatility along its longitudinal axis. We propose and test in healthy subjects an innovative automated approach, which tracks the IVC movements registered in a B-mode US video-clip and estimates the pulsatility of an entire portion of the vein rather than of a single arbitrary section. Large variations of CI estimations were found along the longitudinal axis (in the worst case, CI ranged between 15% and 60%), indicating the importance of investigating a whole portion of the vessel.

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Keywords: Inferior vena cava, Ultrasound, Tracking, Caval index

1 **Introduction**

2 A non-invasive, widely adopted method to assess the intravascular volume
3 status is based on the pulsatility of the diameter of the inferior vena cava
4 (IVC), estimated from ultrasound (US) measurements. It found applications
5 in both healthy subjects (Pasquero et al. (2015)) and conditions of altered
6 volemic status in patients (Lichtenstein (2005)). However, standardization of
7 the measurement technique is still lacking (Wallace et al. (2010)). Different
8 recommendations have been proposed on where to measure the vein diameter
9 along a longitudinal section (Wallace et al. (2010), Resnick et al. (2011)).
10 However, the pulsatility of the IVC along its longitudinal axis may not be
11 homogeneous (Mesin et al. (2015)). As a result, diagnostic recommendations
12 are non-uniform (Zhang et al. (2014)).

13 Pulsatility is measured in terms of the caval index (CI), reflecting the vari-
14 ations of vessel diameter during the respiratory cycle (Blehar et al. (2012)).
15 However, during respiration, the vessel moves relative to the transducer, in-
16 ducing an additional source of variability in the assessment of pulsatility. For
17 instance, the M-mode technique allows to monitor changes in IVC diameter
18 along a fixed line, which is actually fixed with respect to the probe, but may
19 fluctuate with respect to the vessel, depending on respiratory movements
20 (Mesin et al. (2015)). Correspondingly, large movement artefacts are pro-
21 duced, particularly if the vein has an irregular shape (Lichtenstein (2005))
22 or if it rotates.

23 In a recent paper (Mesin et al. (2015)), we proposed a method for tracking
24 IVC movements in long-axis US scans and estimating its diameter in each
25 frame, along a direction moving together with the vein. This approach has a

26 low computational cost and provides a more reliable estimation of IVC local
27 pulsatility than the standard method (Mesin et al. (2015)). However, the
28 pulsatility along a single section may be not representative of the dynamics
29 of the whole IVC. For example, some parts of the vein can show low pulsations
30 for being anchored to nearby structures (e.g., the diaphragm or vein inlets)
31 (Wallace et al. (2010)).

32 The non-homogeneous pulsatility of the vessel and the lack of consensus
33 on an optimal measuring site (Wallace et al. (2010), Resnick et al. (2011)) are
34 likely to contribute to the contradicting indications found in the literature
35 (Weekes et al. (2012)). However, investigations on the pulsatile behavior of
36 the IVC at different longitudinal sites have seldom being reported and were
37 never based on simultaneous monitoring of a whole IVC segment because
38 of lack of the necessary computational tools. Here, we propose a new algo-
39 rithm that tracks the movements and simultaneously monitors the diameter
40 of different sections of a whole portion of the IVC.

41 **Materials and Methods**

42 An algorithm (implemented in MATLAB R2018a, The Mathworks, Nat-
43 ick, Massachusetts, USA) was developed to process each frame of an US
44 B-mode video-clip of a longitudinal view of the IVC. Continuous measure-
45 ments of the diameters along a whole portion of the IVC were computed after
46 compensating for possible IVC movements.

47 At the first frame of the clip, the user is asked to provide the following
48 information used by the software for further processing (Figure 1).

- 49 1. A rectangular portion including a longitudinal view of the IVC is se-

- 50 lected.
- 51 2. On this sub-image, the user selects two reference points, assumed as
52 anchoring sites for the vein. The two reference points are connected by
53 a reference segment. The reference point on the left is usually close to
54 the confluence of the hepatic veins into the IVC, the right one is near
55 the lower hepatic region (caudate lobe) or at the confluence between
56 the IVC and the portal vein.
 - 57 3. The user then draws the leftmost and rightmost segments cutting the
58 IVC transversally, along which the first and last diameter measure-
59 ments are computed (in Figure 1, they are a few mm proximal to the
60 confluence of the hepatic vein and close to the lower region of caudate
61 lobe, respectively). The user is then asked to select two points close to
62 the borders of the IVC along the leftmost section.

63 The software then draws a number of lines (21 in this paper) uniformly
64 distributed between the leftmost and rightmost borders set by the user.
65 Specifically, the lines are at the same distance from each other and their
66 slopes vary linearly between those of the two lines originally selected by the
67 user. The vein borders are then identified along each of these lines as de-
68 scribed in (Mesin et al. (2015)), by detecting sharp changes in the intensity
69 of the US image (which was first processed by a median filter with a square-
70 shaped mask of 9x9 pixels, in order to smooth the image while still preserving
71 edge locations). As more than one point can show a sharp change of intensity
72 along a given section, the one closest to the borders identified in the previ-
73 ous line was considered. For the leftmost line, this method cannot apply:
74 for this reason, the user is asked to select points close to the border in the

75 first frame, as mentioned above; moreover, for the subsequent frames, the
76 borders identified in the previous frame on the first line were used. Once the
77 superior and inferior IVC borders have been estimated along all intersecting
78 lines, their profiles were further adjusted by a longitudinal smoothing, which
79 compensates for minor estimation errors (e.g., noise in the US image, US
80 artefacts such as reverberation and shadowing). Specifically, for each line,
81 the border position was re-calculated as the mean between its original value
82 and the linear interpolation with its two nearest neighbours.

83 The movements of the vein were tracked assuming that they were smooth
84 in subsequent frames. Moreover, small linear deformations were considered.
85 The position of each reference point was automatically re-mapped in subse-
86 quent frames. An estimation of the displacement exhibited by a reference
87 point from one frame to the next was obtained from the comparison of image
88 portions (size 128x128 pixels) centred on the current position of the refer-
89 ence point in the first frame of the pair. The two portions were aligned in
90 the 2D Fourier domain, to improve resolution (Mesin et al. (2015)). The
91 same method as in (Mesin et al. (2015)) was considered, but the image por-
92 tion to be aligned was decomposed into 5 sub-regions. The translations of
93 all regions were computed and their mean translation and rotation were es-
94 timated. Moreover, from the third frame on, three images were considered
95 (the present one and the two previous frames): the movements from each
96 pair of images were computed imposing that the displacement between the
97 first and the last was the sum of the two displacements from the first to
98 the second and from the second to the third. This procedure was found to
99 provide smoother and more stable movements tracking than using only pairs

100 of subsequent frames.

101 Given the new positions of the reference points, a new reference segment
102 was calculated, which could appear translated, rotated or stretched compared
103 to the previous frame. On this basis, each line along which to estimate the
104 IVC section was re-calculated by keeping constant the angle of intersection
105 as well as the ratio of the distances between the intersection point and the
106 two reference points. In this way, these lines followed movements and defor-
107 mations of the IVC and, ideally, always intersected the IVC along the same
108 cross-sections.

109 The superior and inferior borders of the IVC along each line and for each
110 frame obtained as detailed above were affected by high frequency and quan-
111 tization noises. To improve them, the time series (representing the position
112 of each point of the borders over time) were low pass filtered with a cut-off
113 frequency of 4 Hz (this filter and the ones mentioned below were of Butter-
114 worth type, order 4 and used twice, once with time reversed, to remove phase
115 distortion and delay).

116 Then, the vessel midline was computed as the average between the two
117 borders. It was then approximated by a polynomial function of order 4
118 (hereinafter, the term IVC midline indicates this polynomial approximation).
119 Then, 10 points were uniformly distributed along the midline of the vein,
120 excluding the first and last 5% of the curve, to avoid possible edge effects.
121 Then, the sections orthogonal to the IVC midline passing from each such
122 points were considered. The IVC diameters in these sections were computed
123 by interpolation from the estimated vein borders (sampled on the 21 sections
124 considered by the software). Specifically, the two samples of the considered

125 border closest to the line orthogonal to the IVC midline were identified; then,
126 the line passing through these two samples was computed; the intersection
127 point between such a line and the one orthogonal to the IVC midline was
128 then found. Notice that, in this way, the direction along which to compute
129 the IVC sections was standardized as suggested in (Pasquero et al. (2015)).
130 These ten diameters were further considered in the following.

131 In each IVC section, pulsatility was quantified by the CI, defined as the ra-
132 tio between the range of the estimated diameter time series and its maximum
133 (Mesin et al. (2015)). CI values were computed from each respiration cycle
134 (identified based on the low frequency oscillations of the diameter time series
135 appearing after low pass filtering at 0.4 Hz) and their values were averaged
136 obtaining a single index of pulsatility for each section. From these estimates,
137 different indexes could be computed to characterize the overall pulsatility:
138 the mean pulsatility defined as the mean of the CIs in the different longi-
139 tudinal sections; the maximum CI, which could indicate possible collapse of
140 the vein; the standard deviation of the CIs, indicating the variability of the
141 dynamics along the longitudinal axis.

142 The method was tested on the same data as (Mesin et al. (2015)) (to which
143 the reader is invited to refer for the details), i.e., on four healthy subjects
144 in supine position during quiet normal breathing (investigated following the
145 tenets of the Declaration of Helsinki). Additional tests are shown in the
146 Supplementary Material. Pulsatility was measured in terms of the CI of
147 each of the 10 sections orthogonal to the longitudinal axis mentioned above.
148 The distribution of these CI estimates was then shown in boxplots, showing
149 median, quartiles and range.

150 **Results**

151 Figure 1 shows the data provided by the user (location of the vein, refer-
152 ence points and left/right range of interest) and the procedure employed by
153 the algorithm to process each frame.

154 Figure 2 shows an example of processing of data from a subject with
155 an IVC with an irregular profile. The displacement of the vein and the
156 time series of the diameters (measured at different locations along the IVC
157 axis) are shown in 2A and 2B, respectively. Notice the large variability of
158 section sizes along the axis of the vein. Two frames corresponding to local
159 minimum and maximum of average section of the vein are shown in 2C and
160 2D, respectively.

161 Figure 3 shows the results of the processing of the video-clips from the
162 four subjects. The pulsatility was estimated in terms of CI, which was com-
163 puted for each of the 10 sections considered. The boxplot in 3A shows, for
164 each of the four subjects, the distribution of the CI values. Notice that the
165 distributions are very different across subjects. Specifically, subject 4 shows
166 the minimum variations of CI along the axis, with a range of about 19-26%;
167 on the other hand, subject 3 shows the maximum variation of CI along the
168 axis, with values ranging between 15-60%. Minimum and maximum IVC size
169 is shown for these two subjects in Figure 3B. Notice that subject 4 has an
170 IVC with about constant section that indeed pulsates uniformly, whereas the
171 vein of subject 3 shows low and high pulsatility at proximal (left) and distal
172 (right) IVC sites, respectively.

173 **Discussion**

174 *The need of exploring an entire portion of IVC*

175 Diameter oscillations of the IVC are not always homogeneously exhibited
176 in the tract of the vein observed in longitudinal scans, especially in the case
177 of non-uniform appearance. For example, the retrohepatic IVC may be an-
178 chored to other structures, like the diaphragm or hepatic vein inlet with a
179 consequent irregular collapse. Two subjects out of the four considered here
180 showed large variations of pulsatility in the different sections (subjects 2 and
181 3, Figure 3). Additional tests are shown in the Supplementary Material,
182 where other 10 healthy subjects are investigated. Most of them show large
183 variations of IVC pulsatility in different longitudinal sections.

184 This paper proposes a method to investigate automatically the pulsatility
185 of the IVC in an entire portion along the longitudinal course of the vein. The
186 algorithm is an extension of the method proposed in (Mesin et al. (2015)),
187 which describes the tracking of the vein for the assessment of CI along a sin-
188 gle IVC section. As compared to the standard CI assessment, based on US
189 scans in M-mode configuration, IVC tracking proved to considerably reduce
190 artefacts due to the displacements of the vein in connection with movements
191 of the diaphragm (Mesin et al. (2015)). In addition to vein tracking, the
192 novel algorithm allows to compute IVC borders in a region of interest, which
193 can span several centimetres, depending on the subject's echogenicity. By a
194 post-processing, it is also possible to estimate the pulsatility along an opti-
195 mal direction, i.e., orthogonal to the midline of the vessel (Pasquero et al.
196 (2015)). On the other hand, with the standard M-mode approach, the direc-
197 tion of the M-line is constrained to originate from the probe and may thus

198 intersect the IVC along a sub-optimal direction. Notice also that, by using
199 the single diameter studied in (Mesin et al. (2015)), it is not easy for the
200 operator to select a line orthogonal to the midline, whereas it is simple to
201 compute it automatically once the IVC borders are available on an entire
202 portion of the vein along the longitudinal direction. Finally, the possibility
203 to simultaneously collect and average the CI from the different sections along
204 the displayed IVC segment reduces the uncertainty related to the arbitrary
205 choice of a given single section, as done in standard CI assessments.

206 *Perspectives*

207 The proposed algorithm opens new perspectives in the study of IVC pul-
208 satility. For instance it makes possible to investigate whether the IVC ex-
209 hibits systematic changes in pulsatility along the longitudinal axis. In ad-
210 dition, a global CI can be conceived, as the average of the CIs obtained in
211 the different IVC sections, which may possibly yield a more objective and
212 repeatable estimation of IVC pulsatility than the standard approach. This
213 issue is currently under investigation and preliminary results support the
214 hypothesis (Mesin et al., unpublished observations on 10 healthy subjects
215 investigated twice by three operators). Further analysis of the multi-section
216 IVC monitoring may also include the distinct assessment of the respiratory
217 and cardiac oscillatory components (extracted by filtering the diameter time
218 series on specific bandwidths). While the latter has already been the object
219 of some investigation (Folino et al. (2017), Nakamura et al. (2013)), the res-
220 piratory component has not previously been studied. Moreover, the global
221 CI was found to be correlated with the right atrial pressure and useful for its
222 non-invasive estimation, on the contrary of the standard pulsatility estima-

223 tions (Mesin et al., unpublished observations on about 50 patients undergoing
224 right heart catheterization for measuring the atrial pressure). Finally, recent
225 works in progress indicate that there is a good correlation of the average CI
226 (as an overall pulsatility index) with the volemic status of patients (prelimi-
227 nary study on 64 patients either hypo-, eu- or hyper-volemic).

228 *Limitations and possible future improvements*

229 The algorithm is not fully automated, as a few interactions with the user
230 are required to run the processing. In particular, the small area containing
231 the vein needs to be indicated. This preliminary step could be removed
232 by including a method able to identify the IVC automatically (Chen et al.
233 (2018)).

234 Moreover, the user has to indicate two reference points, which should be
235 easily tracked. Automated detection of points with maximal discrimination
236 and invariant under different transformations could be obtained considering
237 standard image matching techniques, e.g., based on Harris detector, scale
238 invariant feature transform (SIFT) or speed up robust feature (SURF) (Riha
239 et al. (2018)). An alternative could be using the popular speckle noise track-
240 ing to estimate the full motion of the vessel (Krupa et al. (2007)).

241 The present semi-automated implementation opens the problem of assess-
242 ing the repeatability of the results when the software is run many times, with
243 different inputs. A general assessment is not possible, as the output depends
244 on the specific video-clip and on the actual portion of vein which is selected
245 by the user. However, as a preliminary test, the same video-clip (i.e., the
246 one recorded from subject 3, showing the largest variations) was processed
247 8 times, considering different selections of input data. The estimated dis-

248 tributions of CI were very similar. Indeed, the following parameters were
249 extracted from them (given in terms of mean \pm standard deviation): mean
250 0.416 ± 0.027 , median 0.447 ± 0.028 , standard deviation 0.168 ± 0.013 , range
251 0.454 ± 0.033 .

252 A more important limitation is related to the separation between the
253 US recording and the off-line processing. This introduces a delay in the as-
254 sessment and also it does not provide immediate feedback about whether
255 the quality of the US imaging is adequate for the processing. This prob-
256 lem could be solved by a real time algorithm embedded into the US system,
257 which would provide the rendering of the estimated IVC borders, guiding
258 the operators in the acquisition of optimal video-clips. The embedding of
259 the software in a US machine requires to reduce the computational time.
260 The present implementation (sequential, interpreted code, implemented in
261 MATLAB R2018a), when run on an average personal computer (with In-
262 tel(R) Core(TM) i7-7500U, Double-Core, clock frequency of 2.9 GHz, 8 GB
263 of RAM and 64 bits operating system), took about 400 ms per frame (i.e.,
264 about 2 minutes to process a video-clip of 300 frames as those considered
265 here). The processing time could be largely reduced by considering a com-
266 piled implementation embedded on a US machine with a powerful processor
267 (a parallel implementation on a GPU or an FPGA could also be considered).
268 Notice also that the frequency range of the investigated signal is of a few Hz,
269 so that the video-clip could be sampled with a frame rate of about 10 Hz,
270 reducing further the computational cost.

271 **Conclusions**

272 We introduced an algorithm to track the movements and identify the
273 borders of an entire portion of IVC in long axis US scans. The proposed
274 method helps to 1) reduce movement artefacts, 2) improve objectivity in the
275 assessment of IVC pulsatility (as the arbitrary choice of a single IVC section
276 is eliminated as well as the choice of the respiratory cycle, as different sections
277 are automatically studied and all breath cycles are identified and the IVC
278 pulsatility is averaged across them), 3) improve stability and accuracy of the
279 estimation by measuring perpendicularly to the vessel axis.

280 Simultaneous monitoring of several sections of a whole IVC segment sig-
281 nificantly extends current US capabilities, providing a longitudinal descrip-
282 tion of IVC size and pulsatility and revealing possibly relevant regional dif-
283 ferences in its elastic behavior.

284 An instrument implementing the algorithm described in this paper was
285 recently patented by Politecnico di Torino and Università di Torino (patent
286 number 102017000006088).

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328 **Figure Captions**

329 **Figure 1:** Example of user setting (A-C) and automated processing (D-E)
330 on the first frame of a US video-clip showing a longitudinal view of the
331 IVC. A) Selection of a rectangle including the IVC portion of interest.
332 B) Enlargement of the selected portion, used for further processing.
333 C) Reference points (squares), leftmost and rightmost sections of inter-
334 est (continuous lines) and points close to the vessel edges along the
335 leftmost section (indicated by circles). Based on these settings, the
336 program defines the reference segment (dashed line) used to track the
337 IVC displacement in subsequent frames. Notice that the image was
338 filtered (by a median filter). D) Automated processing of the algo-
339 rithm: 21 lines are uniformly distributed between the extreme sections
340 indicated by the user. Along these lines, the profile of the vein is iden-
341 tified (the estimated border points are indicated with small circles). E)
342 Post-processing: from the estimated border of the vessel, the midline
343 is computed and interpolated with a polynomial function of order 4
344 (curvilinear line); ten equidistant points are selected on this function
345 and new lines perpendicular to it are considered as sections along which
346 the vein diameters are evaluated (border points indicated with small
347 circles).

348 **Figure 2:** Example of processing of a video-clip. A) Displacement of the
349 IVC shown in terms of the trajectory of the centroid of the reference
350 segment. B) Diameters of 10 sections of the IVC orthogonal to the mid-
351 line of the vessel (grey lines) and mean value (black line). C) Frame of
352 the video-clip corresponding to a local minimum of the average section.

353 D) Frame of the video-clip corresponding to a local maximum of the
354 average section.

355 **Figure 3:** Results of the processing of video-clips from four subjects. A)
356 Distributions of CI along the IVC axis, for each subject (showing me-
357 dian, quartiles and range). B) Two frames of the video-clips of the
358 subjects showing minimum and maximum CI variability (subject 4 and
359 3, respectively).

360 **SUPPLEMENTARY MATERIAL**

361 Results in addition to those shown in the paper are here presented. Ultra-
362 sound (US) data were recorded from other 10 healthy volunteers (5 females,
363 5 males; age, mean \pm std 30 \pm 13 years, height 172 \pm 12 cm, weight 63 \pm 11 kg)
364 with a SonoSite M-Turbo system (SonoSite, Bothell, USA; frame rate 30 Hz,
365 resolution about 0.4 mm per pixel, 256 grey levels) equipped with a convex
366 2-5 MHz probe. Two-dimensional (B-mode) longitudinal views of the inferior
367 vena cava (IVC) were taken with a subxifoideal approach, with the subject in
368 the supine position during relaxed normal breathing. All subjects provided
369 written informed consent for the collection of data and subsequent analysis,
370 according to the Declaration of Helsinki. The experiment was conducted
371 within a study on the repeatability of IVC pulsatility estimation (mentioned
372 in the section Perspectives within the Discussion of the main part of the
373 paper). Different operators repeated twice the acquisition of US video-clips,
374 but only single measurements from a single operator are here considered.
375 The distributions of the caval index (CI) measured along different sections
376 (orthogonal to the estimated axis of the IVC) are shown in Figure I, for each
377 subject. The CI distributions indicate that there is a large variability among
378 subjects: some of them exhibit little variability of pulsatility along the vessel
379 (like subject number 9) and others have large variations (e.g., subjects 5 has
380 a range of CI of about 25-80% and subject 6 shows a CI range of about
381 25-95%). These additional results further support the main thesis of the pa-
382 per: a careful characterization of the dynamics of the IVC requires exploring
383 an entire portion of the vessel, otherwise the assessment of the patient will
384 strongly depend on the specific section considered.

385 **Figure Caption**

386 **Figure I:** Distribution of CI (median, quartiles and range) considering dif-
387 ferent longitudinal sections for 10 healthy subjects.