Influence of Acute Anterior Cruciate Ligament Deficiency in Gait Variability

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The objective of this study was to compare the gait variability of patients with isolated anterior cruciate ligament (ACL) deficiency (experimental group) with that of healthy individuals (control group). The hypothesis was that the gait variability of the experimental group would be higher than the control group. The experimental group consisted of 20 men with an ACL tear and the control group consisted of 20 healthy men without any neurological and/or musculoskeletal pathology or injury. The gait acceleration signal was analysed using the Gait Evaluation Differential Entropy Method (GEDEM). The GEDEM index of the experimental group in the medio–lateral axis was significantly higher than that of the control subjects. A receiver operating characteristic (ROC) analysis was used to assess the diagnostic value of the method and to determine a cut-off entropy value. The GEDEM cut-off value had a 95.6% probability of separating isolated ACL patients from healthy subjects.

KEY WORDS: ANTERIOR CRUCIATE LIGAMENT; DEFICIENCY; DIFFERENTIAL ENTROPY; GAIT ANALYSIS; VARIABILITY

Introduction

Functional ability has a significant impact on quality of life. Many tools have been used for the assessment of functional ability, such as photogrammetric, kinematic and kinetic analyses, video recording, electromyography, force plate analysis, footswitch system, questionnaire tools and validated functional tests.1 – 11 These approaches are time-consuming, specialized, expensive and they demand a complicated laboratory set-up.12 – 14 Accelerometry is a low-cost, repetitive, and practical method of objectively evaluating human movement, with negligible effects on body behaviour. Acceleration of the body or individual body parts can be recorded with no exposure to any radiation, cost-effectively, repetitively and objectively for subsequent analysis.15,16 Accelerometry has been proven to be reliable and highly applicable in the clinical setting,17 – 19 and it has been used to monitor a range of different movements, including gait, sit-to-stand transfers, postural sway and falls. A wide range of measures, including classification of movements, assessment of

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physical activity level, estimation of metabolic energy expenditure, assessment of balance, gait and sit-to-stand transfers can be reliably obtained using a single tri-axial accelerometer worn at the waist. There is a wide variety of accelerometry tools used to estimate human movement and some of them are useful tools in clinical practice. For example, trunk gait accelerometry was reported as being able to reveal even minor changes in normal walking due to different motor strategies in healthy adults, without having an effect on step and stride length and cadence and, therefore, changes in gait.

Entropy is a measure associated with the uncertainty of a system. At the beginning of the 19th Century, Carnot introduced entropy in thermodynamic machines and associated it with temperature and heat. In the later part of the 19th Century, Rudolf Clausius presented the first-ever mathematical formulation of entropy, Boltzmann stated for the first time the logarithmic connection between entropy and probability, and Gibbs established the statistical definition of entropy that is considered to be the most fundamental definition. In the mid 20th Century, Shannon formulated the information theory of entropy.

Biosignals with high probability for periodical behaviour are characterized by low differential entropy. Contrarily, biosignals following a random distribution have higher values of statistical entropy. The entropy of a system is associated with the uncertainty of the result. In human movement, it is possible to use entropy as an index to estimate the uncertainty in walking. Low entropy values are equivalent to more repeatable movements, providing a measure of the precision of movement that a subject is able to perform. High entropy values are associated with the inability of a subject to repeat movements regularly.

Papadakis et al. proposed a new algorithm (the Gait Evaluation Differential Entropy Method [GEDEM]) for processing gait acceleration data, based on the statistical definition of differential entropy. As indicated by GEDEM, lumbar spinal stenosis (LSS) patients exhibit higher gait variability and irregularity in the frequency domain than healthy subjects. The increased gait variability in the frequency domain was attributed to the symptoms of LSS (i.e. acute radicular pain and neurological claudication). The GEDEM method is also useful in monitoring patients with LSS, providing data that show a statistically significant change in pre- and post-operative GEDEM values.

In the present study, the GEDEM index of patients with acute isolated anterior cruciate ligament (ACL) deficiency was calculated. This GEDEM index was then compared with the GEDEM index of healthy individuals (with no ACL deficiency, or other musculoskeletal and/or neurological problems) in order to derive GEDEM values that characterize an acute isolated ACL rupture.

The ACL plays an important role in maintaining the integrity of the knee joint during the support period of gait. This is due to the mechanical properties of the ligament, as well as to the information given to the central nervous system from the mechanoreceptors that are present in the ACL. Unfortunately, rupture of the ACL is a common injury to the soft tissue of the knee. If the ACL is ruptured, the individual may compensate by altering their gait mechanics to reduce the instability of the accompanying knee. It is well known that loss of the ACL is associated with excessive anterior translation of the tibia. Additionally, ACL rupture has been related to alterations in joint movement patterns.
during locomotion.\textsuperscript{35 - 37} Differences in the gait pattern of subjects after ACL injury have been assessed in a number of studies, all using different techniques.\textsuperscript{35,36,38}

The loss of ACL function has been shown to lead to increased mechanical instability of the knee.\textsuperscript{39 - 41} Berchuck \textit{et al.}\textsuperscript{35} described the absence of a net external knee flexion moment at mid stance during level walking in patients with ACL deficiency.

Accelerometry has never been used for the detection of gait variability concerning ACL deficiency. GEDEM is already used for detecting LSS subjects in the general population. The present study was designed to test the hypothesis that individuals with acute isolated ACL rupture would display different entropy values in free-walking speed compared with healthy controls. Furthermore, the ability of the GEDEM method to distinguish subjects with acute ACL deficiency from healthy controls was examined.

\section*{Patients and methods}

\subsection*{SUBJECT SELECTION CRITERIA}
Two groups of males participated in this study; the experimental group consisted of subjects with acute isolated ACL rupture, originally diagnosed by medical staff of the Clinic of Sports Medicine at the Medical Centre of Athens (Maroussi, Attiki, Greece). The control group comprised healthy subjects (university students and staff) with no history of neuromuscular and/or musculoskeletal pathology or injury. The measurements were accomplished from November 2008 to April 2009. The subjects with isolated ACL rupture were initially diagnosed by clinical examination and the diagnosis was confirmed by a subsequent magnetic resonance imaging scan.

Medical history and physical examination forms were completed.\textsuperscript{42,43} Medical doctors were responsible for recording each subject's history including surname, first name and father's name, gender, occupation, height, weight, age and medical history. All subjects signed an informed consent form according to the Bioethics Committee of the University Hospital of Heraklion, University of Crete, Crete, Greece (H.C. Crete 9467/3-9-08). For minors, written consent was obtained from their parents/guardians. The Ethics Committee of the University Hospital of Heraklion, University of Crete (Voutes, Crete, Greece) approved the experiments.

\subsection*{DEVICE DESCRIPTION}
The measurement device consisted of a tri-axial 12-bit digital output linear accelerometer sensor (LIS3LV02DQ), an 8-bit microcontroller (ATTINY2313), a voltage regulator (MC33269D3,3), a 4 MB flash memory, a transceiver and a battery. The accelerometry measurement device was developed at the Technological and Educational Institute (TEI) of Crete, Crete, Greece. The Micro Electro-Mechanical Systems (MEMS) accelerometer sensor was capable of measuring accelerations up to $\pm 2 \, g$. The dimensions of the device were $125 \times 65 \times 25$ mm. The device's low weight (150 g including battery) was important to minimize interference with the measurements. The maximum sampling rate of the measurement device was 2000 Hz. The data were initially stored on a memory card in the measurement device and then they were transferred through an RS232 port onto a personal computer (if an RS232 port was not available a USB to serial adaptor was used). The data were stored on a personal computer in ASCCI format. The data acquisition software was developed in LabVIEW edition 8.2.1 (National Instruments Corp., Austin, TX, USA); the TEI
of Crete (Crete, Greece) obtained a license for using this specific software/edition. The sampling frequency in this study was selected at 128 Hz.27

In the present study, although all accelerations were recorded, only the data from the medio–lateral (y-axis) and anterior–posterior (x-axis) axes were analysed. Typical raw accelerometer signals of the medio–lateral and anterior–posterior axes are presented in Fig. 1.

MEASUREMENT PROCEDURE
All measurements were performed during the morning. Subjects were instructed to wear light clothing that allowed comfortable movement, and a pair of socks. Medical staff ascertained whether the subjects were calm and not nervous. All necessary precautions were taken to minimize distractions to the subjects during the measurements.

The device was attached to the subject’s body with a flexible belt (Fig. 2) around the waist and held in a stable way – moving on the skin – over the middle of the lower back (the medial lumbar region – the L3 process) and close to the centre of gravity of the human body which is considered central with respect to the sagittal plane.44 The centre of gravity reflects body movements and has an important role to play in maintaining dynamic stability during walking.20,45 The measurement device was designed to produce the minimum

![Image](https://example.com/image.png)

**FIGURE 1:** Typical raw acceleration signals of (A) the medio–lateral axis (y-axis) and (B) the anterior–posterior axis (x-axis)
disturbance to the subject’s walking.

Prior to the gait acceleration measurement, personal anthropometric data, a clinical evaluation and patient histories were recorded on the data acquisition software. All subjects were asked to walk along a 40 m straight, level, hospital walkway at a self-selected and comfortable walking speed. The floor was dry, comfortable and flat. The measurement duration was 30 s and the sampling rate for each axis was 128 Hz. It is noteworthy that the 30-s duration and the walking distance of 40 m were significantly greater than a similar study in the literature.17 At the end of each measurement, the subject approached the computer and the gait acceleration data were transferred from the sensor to the computer through a USB cable. Each acceleration measurement was recorded and processed. The first and last two gait cycles were removed, because it was deemed that acceleration and deceleration would contribute to variability. The procedure was repeated three times for each subject.

The measurements were performed both on the premises of the University Hospital of Heraklion, University of Crete, with the aid of the medical staff from the Orthopaedic Department of the University Hospital of Heraklion, University of Crete (Voutes, Crete, Greece), and the Clinic of Sports Medicine, Medical Centre of Athens (Maroussi, Attiki, Greece).

ACCELEROMETER DATA ANALYSIS

The differential entropy signal was calculated using the method developed by Papadakis et al.26,27 Differential entropy is an extension of Shannon’s Entropy to continuous variables. Differential entropy is defined28 as:

\[ h(x) = -\int_a^b f(x) \log_e(f(x)) \, dx \]

where \( f(x) \) is the probability density function of the continuous variable \( x \). Because in most cases it is very difficult or impossible to determine \( f(x) \), the following equation can be used to approximate numerically the entropy of a continuous variable using a discrete (numerical) approximation:28

\[ h(x) = -\sum_{k=1}^n \delta \cdot f(n \cdot \delta) \cdot \log_e(f(n \cdot \delta)) + \log_e(\delta) \]

where \( \delta \) is a discretization parameter, and \( n \) is an integer that satisfies the following condition \( (n - 1) \cdot \delta < x < n \cdot \delta \).

The above equation approximates the continuous variable with a discrete variable \( n \), however it is invariant to the discretization factor \( \delta \). This is a significant benefit compared to the approximate entropy (ApEn) or multiscale entropy that are dependent on proximity parameters (i.e. parameter \( r \)).

The detection of irregularities in a time series was accomplished by transforming the
signal in the frequency domain through a frequency spectrum analysis using Fast Fourier Transform. The differential entropy was then applied to the power spectrum. A periodic (low variability in the frequency domain) signal indicated a predominant frequency component and, therefore, the differential entropy would be obtained at lower values. On the other hand, a random signal (e.g. white noise) indicated more frequency components with relatively high power and, as a result, higher differential entropy values would be obtained. Thus, low spectral differential entropy values were associated with a periodic gait acceleration time series, while high spectral differential entropy values were associated with an irregular gait acceleration time series.

Depending on the logarithmic base, differential entropy is measured in bits for \( \log_2 \), nats for \( \log_e \) and bans for \( \log_{10} \). Base selection does not qualitatively change the results. The base selected in this study was \( \log_e \) and, therefore, used nats as the units of differential entropy.

Each measurement was processed separately through the custom-developed analysis software. A GEDEM index was calculated for the anterior-posterior and medio-lateral acceleration axes for every measurement and the mean GEDEM value was calculated from three measurements.

STATISTICAL ANALYSIS
All analyses were carried out using the SPSS® statistical package, version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows®. A t-test was used to determine statistically significant differences in the mean values of age, height, weight and body mass index (BMI) between the two groups of subjects. A t-test was also used to compare the spectral differential entropy values between the two groups (the null hypothesis was that the mean values were equal). A receiver operating characteristic (ROC) analysis was used to determine the optimal cut-off differential entropy point for separation of patients and control subjects and to estimate the percentage of true positives. In order to assess the diagnostic value of the method, the likelihood ratio (LR) was used. A positive LR (PLR) is defined as sensitivity/(1 – specificity) and expresses the probability that a positive test result would be expected in a patient with (as opposed to without) ACL rupture. A high PLR (e.g. 5.0) indicates a test in which a positive result is helpful for ruling in the diagnosis. A negative LR (NLR) is defined as (1 – specificity)/sensitivity and expresses the probability that a negative test result would be expected in an ACL patient. A small NLR (< 0.3) is associated with tests in which a negative result is helpful in ruling out a diagnosis. All tests were two-sided and statistical significance was set at \( P < 0.05 \).

Results
SUBJECTS
Table 1 presents the anthropometric characteristics of the two study groups. The experimental group consisted of 20 men with acute isolated ACL rupture who were able to walk for at least 40 s. The control group consisted of 20 healthy men with no history of neurological, musculoskeletal, respiratory or cardiological pathology or injury. There were no significant differences between the two groups of subjects in terms of their anthropometric characteristics.

Table 2 presents the spectral differential entropy values for the experimental and control groups for the medio-lateral and anterior-posterior axes and Fig. 3 presents dot plots of these values and shows the optimal cut-off values for each axis as calculated by ROC curve analysis (see next
The GEDEM index of the experimental group in the medio-lateral axis, but not the anterior–posterior axis, was statistically significantly higher ($t_{38} = 7.652$, $P < 0.0001$) than that of the control group.

### ROC CURVE ANALYSIS
To obtain the ROC curve, a series of cut-off values was created by selecting midpoints through the ordered differential entropy values. For each cut-off (1 – specificity and...
sensitivity), values were computed as percentages based on the true positives and false negatives. A ROC curve represents the coordinates of each set of coordinates of each cut-off value in the two-dimensional space of 1 – specificity and sensitivity. Each point has a distance from the diagonal (the non-discrimination line). The point with the greater distance from the diagonal was selected and indicates the optimum trade-off between true positives and false negatives. To obtain the ROC curve, the differential entropy values were ordered with respect to magnitude. A ROC analysis was followed for each of the two axes. ROC curves of the medio–lateral and anterior–posterior axes results are presented in Fig. 4, respectively. For the medio–lateral axis, the ROC analysis determined the optimal cut-off value as 1.069 nats. Spectral differential entropy values > 1.069 nats (i.e. higher irregularity) indicated ACL deficiency. The cut-off entropy value (1.069 nats) yielded to 90% sensitivity and 85% specificity. ROC analysis estimated a 90% probability for the correct identification of patients and an 85% probability for the correct identification of healthy subjects. According to the ROC analysis, the area under the curve was 95.6%; therefore, the spectral differential entropy index had a 95.6% probability for distinguishing between ACL patients and
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For the anterior–posterior axis, the ROC analysis determined the optimal cut-off value as 0.582 nats. Spectral differential entropy values > 0.582 nats (i.e. higher irregularity) indicated ACL deficiency. The cut-off entropy value (0.582 nats) yielded to 55% sensitivity and 90% specificity. The ROC analysis estimated a 55% probability for correct identification of patients and a 90% probability for correct identification of patients and a 90% probability for correct identification of healthy subjects. The PLR (sensitivity/[1 – specificity]) at the cut-off value was 5.50 and the NLR was 0.18. Thus, the LR values of gait variability (through the spectral differential entropy index) suggested that the method had moderate diagnostic value for using the anterior–posterior axis data, taking the sample size into account.

**Discussion**

Accelerometry and the differential entropy algorithm were used in the present study, for healthy subjects. According to the ROC analysis, the area under the curve was 71.2%; therefore, the spectral differential entropy index had a 71.2% probability for distinguishing between ACL patients and healthy subjects. The PLR (sensitivity/[1 – specificity]) at the cut-off value was 5.50 and the NLR was 0.18. Thus, the LR values of gait variability (through the spectral differential entropy index) suggested that the method had moderate diagnostic value for using the anterior–posterior axis data, taking the sample size into account.

**FIGURE 4:** Receiver operating characteristic (ROC) curves for various thresholds using the differential entropy values of (A) the medio–lateral axis (y-axis) and (B) the anterior–posterior axis (x-axis)
the first time in orthopaedics, to evaluate ACL-affected patients. Many gait analyses studies have utilized accelerometry as it provides quantitative measures of gait that identify specific gait changes in elderly adults and in fallers, and it can be used objectively to quantify ambulatory activity levels.\(^1\) Trunk gait accelerometry was reported as being able to reveal even minor changes in normal walking due to different motor strategies in healthy adults, without any effect on step and stride length and cadence and, therefore, changes in gait.\(^{17,20}\) Accelerometers have also been implanted in hip prostheses and been shown to detect loosening.\(^{48}\) There is a clinical need to develop objective methods of gait evaluation as clinical observations of gait can be subjective, qualitative and sometimes inconsistent, particularly when the observers are not very experienced.\(^49\) Arif et al.\(^{20,45}\) used accelerometers for studying the effect of fatigue on the walking stability of young and elderly subjects.

Some researchers have used accelerometry for analysing gait cycle parameters, such as cadence and step length, with an autocorrelation procedure measuring gait regularity and symmetry.\(^{50}\) Special tests performed in the physical examination of athletes with musculoskeletal injuries require skill, however this does not ensure accuracy.\(^{42}\) Human walking patterns are different. Each person’s gait kinematic and kinetic quantities are assumed to be periodic,\(^{51,52}\) or pseudo periodic,\(^{14}\) and determined by body characteristics and a personal ability to control gait. In the case of neurological and musculoskeletal pathologies or injuries, these movements may not be periodic and may result in increased gait instability. More specifically concerning ACL rupture, knee subluxation and concomitant knee pain compel the subject to compensate by adjusting the gait pattern. This leads to increased gait variability.

In the literature there have been conflicting reports regarding the trend of gait variability in pathological conditions. The increased gait variability observed in the present study was consistent with the findings of a number of studies.\(^{20,45,53-55}\) It has been reported that gait variability increases with increasing age (and, therefore, loss of neuromuscular control).\(^{20,45,53,54}\) Similarly, it has been reported that fall-risk subjects indicate higher minimum foot clearance variability.\(^{55}\)

Georgoulis et al.\(^{56}\) observed that an ACL-deficient knee exhibits more regular and less variable patterns than an intact knee. ACL deficiency is, however, a condition in which the subject is able to adjust his/her walking strategies in order to compensate for the perceived instability. As a result, the subject walks at a pace and with a style that protects the injured knee from a subluxation. In contrast, LSS subjects are only able to react to the radicular pain, which manifests as poorly localized pain.\(^{57}\) The reaction to LSS-induced pain leads to irregular and unpredictable movements, thereby increasing the variability. Thus, according to these studies, LSS-affected patients, when compared to healthy subjects, exhibit radically different gait variability, in contrast with patients having ACL rupture, which exhibit more regular walking patterns than healthy subjects.\(^{27,56}\)

An additional finding of Georgoulis et al.\(^{56}\) was that ApEn values for injured subjects significantly increased with increasing walking speed. As the ACL-affected patient is forced to increase their speed beyond the comfort zone, they lose their ability to apply the strategy that they have developed that protects the injured knee. As a result, the
increased pain leads to irregular movements and increased gait variability in a way similar to LSS-affected patients.

Two possible limitations of the Georgoulis et al. study were that subjects walked on a motorized treadmill instead of solid ground and both males and females were included in the study groups. Some investigators have administered paced walking, where either walking speed is controlled as on a treadmill, or cadence is standardized by a metronome. This practice may, however, affect walking behaviour and, therefore, restrict the validity of results and so it is preferred by different investigators to have the subjects walking at a self-preferred speed without external control. Additionally, it has been shown that there are gender differences in the biomechanical properties of the lower extremities.

Changes in gait variability are also consistent with the reports by Costa et al., who reported that unconstrained free walking has more complex dynamics, followed by fast walking and, finally, slow walking. In general, therefore, gait variability is expected to increase as the subject moves away from the comfort zone, and is expected to decrease if the subject is able to devise and implement successful control strategies to prevent pain, probable new injury or fall.

Gradually progressing or chronic conditions allow an individual to adapt their gait patterns. Dingwell and Cavanagh reported small, but statistically significant, increases in the variability of peripheral neuropathy patients’ movement patterns compared with healthy individuals. The lack of significant differences in long range correlation was attributed to adaptation effects. Peripheral neuropathy is a slowly advancing disease and these patients have been living with significant and progressive sensory loss for many years.

Past studies have shown that subjects with ACL deficiencies alter the manner in which they walk. Normal subjects have an external knee flexion moment during mid-stance (biphasic gait), while ACL-deficient patients often have a decrease in the external knee flexion moment at mid-stance. In addition, some ACL-deficient patients never achieve an external knee flexion moment during mid-stance. This type of gait has been referred to as the ‘quadriceps avoidance gait’. Acute ACL-deficient patients have been shown to exhibit a quadriceps avoidance pattern prior to and 6 weeks following surgery, whereas no quadriceps avoidance pattern developed in chronic ACL-deficient patients. Knoll et al. also found evidence of a quadriceps avoidance pattern that was not observed, because the chronic ACL-deficient and healthy group’s knee position curves paralleled one another throughout stance and showed a flexion–extension–flexion pattern; no significant differences were observed when comparing healthy subjects with those of the control group.

Berchuk et al. observed that acute ACL-deficient subjects showed an increased knee extension during the stance and reduced flexion during the swing phase, and a reduction of medial and lateral quadriceps activity. These findings are supported by results from other studies.

Based on these studies, it is believed that a chronic ACL rupture generates more stability and, therefore, less gait variability during walking than an acute ACL rupture, because of the adaptation mechanisms that are developed. This might explain the difference in results from the present study compared with those shown by other researchers who have investigated gait variability in chronic ACL rupture.

A ROC analysis was performed for each of
two axes in the present study. For the medio-lateral axis, a cut-off value equal to 1.069 nats was determined with a 90% probability for correct identification of patients and an 85% probability for correct identification of healthy subjects. It was estimated that the proposed method has a 95.6% probability for correctly distinguishing between patients with acute isolated ACL deficiency and healthy subjects in the case of the medio-lateral axis. For the anterior-posterior axis, a cut-off value equal to 0.582 nats was determined, with a 55% probability for the correct identification of patients and a 90% probability for the correct identification of healthy subjects. It was estimated that the proposed method has a 71.2% probability for correctly distinguishing between patients with acute isolated ACL deficiency and healthy subjects in the case of the anterior-posterior axis.

During walking, the gait periodicity of a healthy individual is high. On the contrary, the gait of a non-healthy subject will exhibit deviations from the periodic gait. As a result, healthy subjects are characterized by lower GEDEM values, while non-healthy subjects are characterized by higher GEDEM values. The proposed algorithm was able to detect statistically significant differences in gait variability between acute isolated ACL deficiency patients and healthy subjects.

A limitation of the present study was the small number of participants, due to the screening and exclusion of patients with neuromuscular and musculoskeletal injury different to ACL. Another reason for the small number of participants was the absolute requirement for patients with only acute ACL deficiency.

The vertical acceleration signal in the present study was not considered, as it is well known that excessive anterior translation of the tibia has the main influence on stability in the antero-posterior and medio-lateral axes during walking in patients with ACL deficiency.\(^3\),\(^4\)

Gait analysis using accelerometry and differential entropy has the added advantage of causing less stress to the subject, because the analysis can be conducted in a short time and the subject is only required to walk as usual. It permits objective and quantitative evaluation of the gait characteristics in patients with ACL rupture and could be useful for the evaluation of responses to surgical treatment in these subjects. The proposed method is also painless, low-cost, non-invasive, requires no radiation or chemicals, is easy to perform on any solid ground, and the objective index that corresponds to gait irregularity may be computed instantly.

The results from the present study indicate that patients with acute isolated ACL deficiency exhibit higher irregularity in gait patterns than healthy subjects. This result applied only to groups of healthy and ACL-deficient patients (i.e. it would not be possible to discriminate between other gait-affecting pathologies using this method). The proposed method may be used as a cost-effective first stage screening method. Further work and a higher number of individuals are required to improve the performance of the method.

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Conflicts of interest
The authors had no conflicts of interest to declare in relation to this article.
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