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# Quantification of Deformation of the Popliteal Arterial Tract During Leg Flexion in Subjects with Peripheral Arterial Disease: A Pilot Study

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**ABSTRACT**

*Purpose:* To quantify the in-vivo deformations of the popliteal arterial segment (PAS) during leg flexion in subjects with clinically relevant (Fontaine Stage IIb) peripheral arterial disease (PAD).

*Methods*: Five patients with varying calcification levels of the PAS undergoing endovascular revascularization underwent 3D rotational angiography. Image acquisition was performed with the leg straight and with a flexion of 70°/20° in the knee/hip joint. The arterial centerline and the corresponding branches in both positions were segmented to create 3D reconstructions of the arterial trees. Axial deformation, twisting, and curvatures were quantified. Furthermore, the relationships between the calcification levels and the deformations were investigated.

*Results*: We observed an average shortening of the PAS of 5.9% ± 2.5% and twist rate of 3.8 ± 2.2 °/cm. Maximal curvatures in straight and flexed positions were 0.12 ± 0.04 $cm^{-1}$ and 0.24 ± 0.09 $cm^{-1}$ respectively. As the severity of arterial calcifications increased, the maximal curvature in straight position increased from 0.08 $cm^{-1}$ to 0.17 $cm^{-1}$; while an increase from 0.17 $cm^{-1}$ to 0.39 $cm^{-1}$ was observed for the flexed position. Axial elongations and arterial twisting were not affected by the calcification levels.

*Conclusions*: The PAS of patients with symptomatic PAD is exposed to significant deformations during flexion of the knee joint. The curvature is directly affected by the extent of arterial calcification. In contrast, the changes in arterial length and twisting angles are comparable to those of healthy arteries. ~~These measurements have the potential to be used for realistic arterial modeling to improve stent designs.~~This study also showed the ability of rotational angiography to quantify the three-dimensional deformations of the PAS in patients with various levels of calcification, and that this technique can be used to collect data on larger groups of patients.

Key words: popliteal artery, femoro-popliteal arterial segment, 3D rotational angiography, knee flexion, peripheral arterial disease, 3D arterial reconstruction, arterial calcification, axial deformation, maximal curvature, twist rate.

## INTRODUCTION

The obstruction of lower limb arteries, commonly known as peripheral arterial disease (PAD) is mainly caused by atherosclerosis.[1,2] Endovascular therapy is currently considered the primary treatment modality for many PAD patients.[2] Restenosis,[3–5] a narrowing of the dilated artery subsequent to endovascular therapy, hampers clinical outcomes following balloon angioplasty of the femoro-popliteal arterial segment (FPAS) in up to 60% of the patients at one year.[6] Although the introduction of novel Nitinol stents decreased restenosis rates compared to plain balloon angioplasty (POBA),[7] restenosis still remains a significant problem in peripheral arteries.[6,8] In-stent restenosis occurs in up to 30% of the patients subsequent to bare metal Nitinol stent placement[6] and was reported to be associated with stent fractures[9,10] and arterial wall damage.[4,11] Stent failures are clearly associated with the forces exerted on the FPAS, which are caused by bending, torsion and axial motions during hip and knee flexion.[12–14] Moreover, the effects of this mechanical environment, along with different stent designs and material properties, on the stent-artery wall interactions lead to arterial wall damage.[11]

To understand the causes of restenosis and improve stent designs, an accurate characterization of this mechanical environment is necessary. Due to the difficulties arising from in-vivo measurement of mechanical forces, previous studies concerned with this characterization focused on the quantification of in-vivo arterial deformations.[12–18] Although the improvements with each new study are evident, there are certain limitations that may affect their results; namely the use of cadavers[15,16], young[12,17] and healthy subjects,[14,18] and subjects with only mildly or non-calcified arteries.[13] To our knowledge, no data is available concerning arterial deformations in patients with clinically relevant PAD. This information is critical since these patients correspond to the target group for stenting and calcified arteries may deform differently when compared with healthy tissue.

Aim of the present study is to gain a better understanding of the mechanical environment of the atherosclerotically diseased popliteal arterial tract. Based on the above-mentioned limitations of previous studies, it is our understanding that quantifying the deformational change in mild to severely calcified diseased arteries will give a more realistic insight into the mechanical environment created during leg flexion. Furthermore, a better understanding of the biomechanical prerequisites of this complex arterial environment, may ultimately lead to improved stent designs resulting in lower restenosis rates.

## MATERIALS AND METHODS

Images were obtained on a clinical indication on five patients (1 female, mean age 71 ± 9) during endovascular therapy for femoro-popliteal arterial obstructions. Clinical characteristics and risk factors are outlined in Table 1. Ethics committee approval for the present study was not required since patients were treated according to the regular clinical protocol. In addition, all patients signed a general consent form approved by our institutional review board, thereby agreeing on usage of anonymized data for quality control and retrospective studies. For each patient, 3D rotational angiography of the popliteal arterial segment (PAS) was performed (AXIOM-Artis, Siemens, Germany) in two natural lower limb positions: with the subjects' lower limb fully extended and during flexion of the knee. 3D rotational angiography was performed utilizing a standard commercially available dyna CT algorithm on the angiographic workstation. Care was taken to standardize knee flexion in all patients, with the help of a specifically designed cast placed under the patients' legs over which the knees were bent (Fig. 1). The resulting configuration corresponded to a position in normal walking situation with a 70°/20° flexion in the knee joint.[16]

All 3D angiographic examinations were saved digitally and transferred to a workstation (Microsoft Windows operating system) capable of three-dimensional post-processing to quantify the deformation of the arterial tract for each patient. For 4 patients, the investigated segment of the arterial tract started from the descending genicular artery and ended at the superior genicular artery, while it ended at the inferior genicular artery in one patient. Vascular calcification was assessed using a semi-quantitative scoring system [16]: no (0) versus moderate (1) versus heavy calcification (2).

For an accurate quantification of the arterial deformations**,** the obtained images were first subjected to pre-processing. In summary, the patients' vasculature and bone structures were segmented on the 3D image datasets using an image-analysis software (Amira 5.2, Visualization Sciences Group SAS). As a result, the 3D vascular tree was obtained for both flexion angles of the leg (Fig. 2). Based on these three-dimensional reconstructions, corresponding arterial branches were identified on the two positions. Four landmarks were used to establish the 3D correspondences between the reconstructed arteries at the two angles of flexion dividing the artery into three segments that contain two branches each. The centerline of the whole artery and its respective segments were extracted with the skeletonized feature of Amira. B-splines were used to represent the centerlines, which provided parametric representations of the arteries.

The deformations of the arteries during the flexion were quantified with the axial deformation, the twist angle and the curvature of the artery. The procedure used in this study follows standard techniques previously published,[14,18] but will be summarized here.

Based on the splines describing the arterial centerline, the arc length of the arteries was calculated at each flexion angle. The axial deformation was then measured as the change in the lengths of the segments between straight and flexed positions, divided by the total length of the artery (Fig. 3a).

For the twist angle quantifications, the “angle of separation” for each segment was calculated by measuring the angle between consecutive side branches. The angle of separation was measured before and after flexion; the angular change induced by the motion corresponded to the twist angle. In addition, the twist angle rate was calculated by dividing the twist angle by the length of the arterial segment. Since the arteries are not straight, the calculations required to obtain the angle of separation must consider the curvature of the arteries. This calculation is done by division of the arterial centerlines into very short sections, such that each section can be assumed to be lying on a plane. The angle between consecutive sections was calculated and used to compensate for the arterial curvature (Fig. 3b). A detailed description of the mathematical derivation can be found elsewhere.[18]

The arterial curvature was calculated using the osculating circle along the length of the artery. The radius of the circle was defined by three points on the centerline. To avoid measuring insignificant local curvatures, these three points were separated by a distance equal to the arterial diameter. The curvature was defined as the inverse of the radius of the fitted circles. Unlike axial length and twist quantifications, curvatures were calculated along the entire length of the arteries and not for each individual segment (Fig. 3c).

In addition, the relation between the severity of calcification and the deformation metrics were analyzed. Spearman’s rank correlation[19] ($\rho$) was utilized as a statistical analysis to assess the dependence between these parameters. If an increase in one of the parameters leads to either an increase or decrease in the other one, and if this relation can be defined by a monotonic, but not specifically a linear function, Spearman suggests that these parameters have a positive or negative correlation. A correlation coefficient of +1 means a perfect positive correlation. In this study, the deformation metrics were sorted and ranked in an ascending order, as were the patients' corresponding calcification levels.

## RESULTS

Axial length of the PAS decreased during bending of the leg when compared to the straight leg position in all patients (Table 2). Average compression of the PAS for all patients was found to be 5.9% ± 2.5%; while the average maximum compression was 16.4% ± 8.4%. Moreover, we observed twisting of the PAS during leg flexion: The average twist rate was 3.8 °/cm ± 2.3 °/cm, with an average twist angle of 45° ± 25° (in the range of 6° – 71°). The measurements also showed that both the mean and the maximal curvature of the PAS increased during flexion of the leg. Arterial twisting was about two times higher after flexion of the knee joint (mean: 0.12 $mm^{-1}$ ± 0.07 $mm^{-1}$ ; maximal: 0.24 $mm^{-1}$ ± 0.09 $mm^{-1}$) when compared to the curvature measured in the straight position (mean: 0.06 $mm^{-1}$ ± 0.02 $mm^{-1}$; maximal: 0.12 $mm^{-1}$ ± 0.04 $mm^{-1}$).

The level of calcification increased from mild to severe among the patients considered. A strong positive correlation was observed between the maximum curvature and the level of arterial calcification, with a ρ factor of 0.97 and 0.98 for straight and flexed positions, respectively (Fig. 4). The same correlation was observed between the mean arterial curvatures and the calcification with a ρ factor of 0.98 for both straight and flexed positions. On the other hand, no relationship between the extent of arterial calcification and axial compression or arterial twisting was observed (calculated correlation ρ of 0.40 and 0.43, respectively).

## DISCUSSION

The FPAS is a very challenging territory for endovascular therapy and especially for the placement of stents.[2,6] Excessive biomechanical deformations may constitute possible explanations for the limited success of stents in these arterial segments.[12–14] To provide a deeper understanding about the mechanical environment in popliteal arteries during flexion, arterial deformations of five patients with various levels of arterial calcifications ranging from mild to severe were quantified based on 3D rotational CT imaging.

Our results suggest that flexion of the leg in the knee joint induced a decrease of arterial length, an increase of the curvature as well as substantial amount of twisting in the PAS. Furthermore, an increase in the calcification level led to an increase in the maximal curvature observed in both straight and flexed positions, while no change in the amount of arterial twisting and axial deformation was observed for the different levels of calcification.

A direct comparison of these results with previous publications is difficult due to the use of different methodologies, where healthy volunteers were considered with various mechanical configurations and imaging modalities.[12–18] Although these studies provided important information concerning arterial deformations occurring during various activities, they mostly considered young[12,17] and healthy subjects,[14,18] and subjects with only mild or non-calcified arteries.[13] To our knowledge, the present study is the only one on subjects with clinically relevant PAD; however, the general arterial behavior during the flexion measured in the present work is consistent with previous observations. All published studies reported arterial shortening during leg flexion. The mean amount of shortening reported previously ranges from 15.1% for patients with mild calcifications[13] to 7.4% for healthy subjects[14]. With a 5.9% mean shortening for arteries with moderate to severe calcifications, our measurements showed a slightly lower axial compression. This confirms the decreased elasticity of the artery from young, healthy subjects to older diseased patients. Concerning the mean twist angle between straight and flexed positions, Klein and coworkers [13] observed a change of 61.1º ± 31.9º in the popliteal arteries (PAs) of subjects with mild calcifications.. These findings are on par with the mean change of the twist angle of 45.9° ± 25.4° obtained in the present study. Due to the differences in the lengths of the arterial tracts, the comparison of the twist rate is more important than the mean twist angle. The axial twist rate found in the previous studies was between 1.9 °/cm and  3.46 °/cm for the PAs of patients with clinically different backgrounds.[14]  These results compare favorably with our calculation of 3.8°/cm ± 2.3°/cm, since the amount of deformation applied to the leg was in the lower range of the scale.

Due to a limited number of studies on curvature, a satisfactory evaluation of the results, with regard to their accuracy is challenging. Klein and coworkers [13] quantified the mean curvature of the PA segment in straight leg and crossed leg positions as 0.1 $cm^{-1}$ ± 0.02 $cm^{-1}$ and  0.31 $cm^{-1}$ ± 0.1 $cm^{-1}$. Cheng's findings on curvature vary considerably with respect to the subjects. While no bending was reported in the PAs of healthy, young subjects;[17] a maximal supine curvature of 0.11 $cm^{-1}$ ± 0.05 $cm^{-1}$ and a maximal flexed curvature of 0.47 $cm^{-1}$ ± 0.24 $cm^{-1}$ were observed along the ~~entire~~ proximal PAs of healthy, old subjects.[14] While both our mean and maximal straight curvatures compare with these results, the mean and maximal flexed curvatures of 0.12 $cm^{-1}$ ± 0.07 $cm^{-1}$ and 24 $cm^{-1}$ ± 0.09 $cm^{-1}$ is lower than the reported values.

This finding may be attributed to slightly more pronounced knee flexion in the compared studies.[13,14]

The comparison of our results with the previous studies suggest that, although there are significant deformations in the PAs of diseased patients during leg flexion, the amount of change observed in the PAD patients does not differ significantly from the ones observed in healthy volunteers.[14,17,18] The differences between the published results are likely to be attributed to anatomical variations between patients. Based on this observation, we may conclude that the level of calcification has a limited effect on both the axial deformation and twisting of the PAs when the leg is flexed. The observed relation between the calcification levels and curvature in both leg positions suggests that as the extent of calcification increases, the curvature of the PA increases. This is in agreement with the observation of Cheng and colleagues[14], which attributes the increased curvature to lower elasticity of arteries impacted by patient age.

One possible and significant use of these measurements with respect to improving the stent designs is in Finite Element (FE) simulations. Since the stents undergo rigorous FE simulations during development, these measurements can be applied as boundary conditions to realistically model the deformation of calcified arteries, even without explicitly modeling the calcification. To our knowledge, the measurements used in the previous FE simulations are all based on cadaveric[20–22] or healthy arteries[12] and ignore any possible effect the calcification level may have on the deformation metrics, contrary to what we have showed in the present study. The use of these measurements in FE simulations might have a role in improving stent designs through the analysis of stent behavior and their fracture mechanics under these deformations.

Several limitations of the present study need to be discussed. First, due to size constraints of the angiographic imaging system, we could not consider the entire length of the FPAS, but concentrated on its distal part. Moreover, space constraints in the angiographic system limited the extent of leg motion. Although the flexed position of the leg considered in this study is one of the most important to consider, the procedure could not be extended to more complex physiological situations. Future studies should consider 2D X-ray image acquisitions, which can cover a larger segment of the artery and also allow for higher flexion angles. Although the deformations along the FPAS are not uniform, most of the deformation is expected to take place in the target region analyzed. Future studies should also consider quantifying the entire femoro-popliteal segment to disregard any effect the sizes of the arteries might have on the results. Another limitation concerns the limited number of patients included; however, the typical number of subjects in similar work is between 1 and a maximum of 10.[12–14,17,18] In addition, the patients considered in this study covered a large range of arterial calcifications, which is sufficient to provide an assessment of the effect of the PAD on the arterial deformations.

## CONCLUSION

The study showed that 3D rotational angiography is a method suitable to accurately quantify the deformation of the PA segment in patients. The available workspace is larger than other 3D imaging systems such as MRI, which enables more realistic range of flexion. In addition, it provides a full three-dimensional representation of the tissue and is not limited to bi-dimensional radiographic projections. ~~of the PAS with~~The measurements were performed on subjects with varying levels of arterial obstruction~~ was performed in both straight and flexed leg positions~~, in both straight and flexed leg positions thereby representing knee joint positions as observed during walking. We observed significant changes in curvature, twist angle and length of the PAS during leg flexion. The quantifications also lead to a relation of a higher curvature with more severe calcification levels. This implies that the calcification directly affects the curvature, while no such relation with twisting or axial deformation was found. This relation supports the idea that the quantifications help to uncover clinically very important information on the deformation mechanics of the lower limb arteries and may give important insight into stent placement and design. The methodology followed in this pilot study proved to be appropriate to achieve accurate 3D quantifications and can therefore be used to collect data on larger groups of patients.

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Table 1: Patient demographics, clinical presentation, cardiovascular risk factor profile and level of calcification

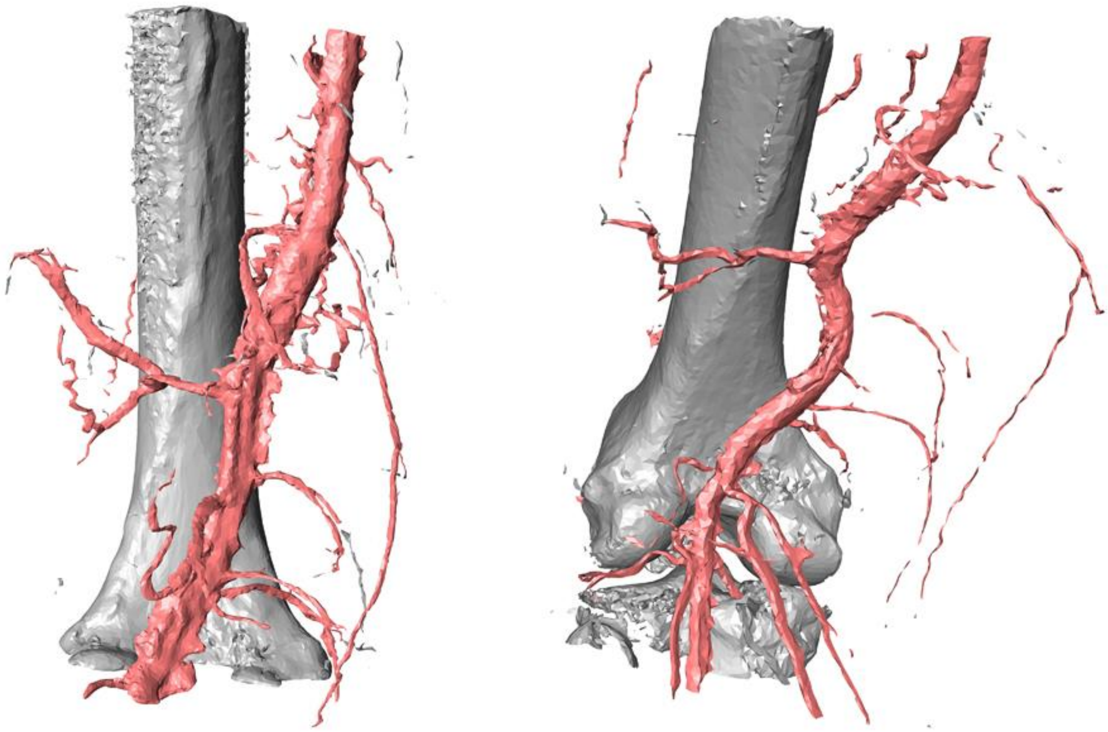
| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|---|---|---|---|---|---|
| Age | 76 | 56 | 65 | 79 | 69 |
| Gender | Male | Male | Male | Male | Female |
| Fontaine stage | IIb | IIb | IIb | IIb | IIb |
| Hyperlipidemia (yes / no) | No | No | Yes | Yes | No |
| Diabetes mellitus (yes / no) | Yes | Yes | No | No | Yes |
| Arterial Hypertension (yes / no) | Yes | Yes | Yes | Yes | Yes |
| Cigarette smoking (yes / no) | Yes | Yes | Yes | No | Yes |
| Coronary heart disease (yes / no) | Yes | No | No | Yes | No |
| Cerebrovascular disease (yes / no) | No | No | No | No | No |
| Creatinine (µmol/l) | 78 | 85 | 89 | 75 | 58 |
| Level of obstruction | Popliteal | Popliteal | Popliteal | Popliteal | Popliteal |
| Calcification | Heavy (Level 2) | None (Level 0) | Moderate (Level 1) | Heavy (Level 2) | Moderate (Level 1) |
| Stenosis versus occlusion | Stenosis | Occlusion | Stenosis | Stenosis | Stenosis |

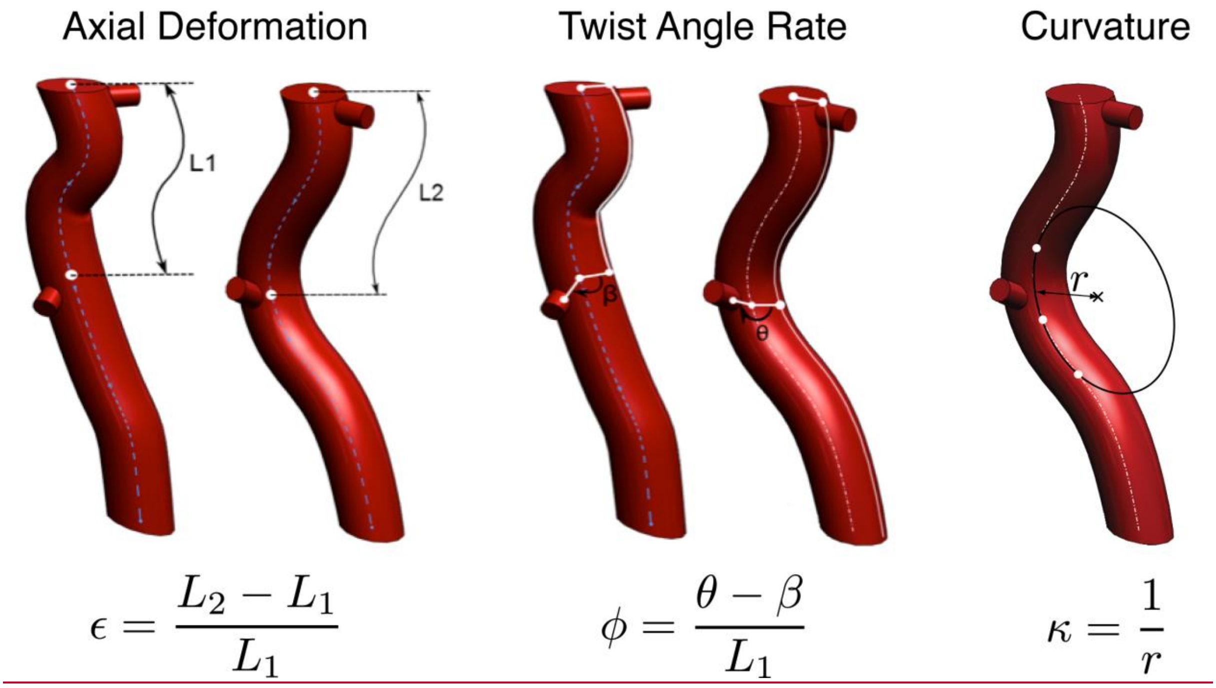
Table 2: Three-dimensional arterial deformations of the popliteal arterial segment during knee flexion in five patients undergoing endovascular therapy; axial compression, twist rate and curvature.

| | Deformation from straight to flexion | | | | Curvature ($cm^{-1}$) | | | |
|---|---|---|---|---|---|---|---|---|
| | Axial (%) | | Twist rate (° /cm) | | Straight | | Flexed | |
| **Patient** | Mean | Max | Mean | Max | Mean | Max | Mean | Max |
| **1** | -4.5 | -27.4 | 5.9 | 13.2 | 0.09 | 0.17 | 0.23 | 0.39 |
| **2** | -7.6 | -23.3 | 5.9 | 10.9 | 0.04 | 0.08 | 0.08 | 0.17 |
| **3** | -6.6 | -9.2 | 0.5 | 1.3 | 0.06 | 0.12 | 0.06 | 0.2 |
| **4** | -8.4 | -11.6 | 4.5 | 8.5 | 0.07 | 0.13 | 0.14 | 0.22 |
| **5** | -2.4 | -10.4 | 2.2 | 4.8 | 0.05 | 0.08 | 0.08 | 0.21 |
| **Mean ± SD** | -5.9 ± 2.5 | -16.4 ± 8.4 | 3.8 ± 2.2 | 7.74 ± 4.8 | 0.06 ± 0.02 | 0.12 ± 0.04 | 0.12 ± 0.07 | 0.24 ± 0.09 |


Figure 1: Positioning of the leg during 3D rotational angiography: Straight (left) and flexed (right) with the help of a cast designed to simulate the walking condition

Figure 2: Threshold-based segmentation of the bone and artery for patient #1 with the leg in a straight position (left) and after flexion (right)





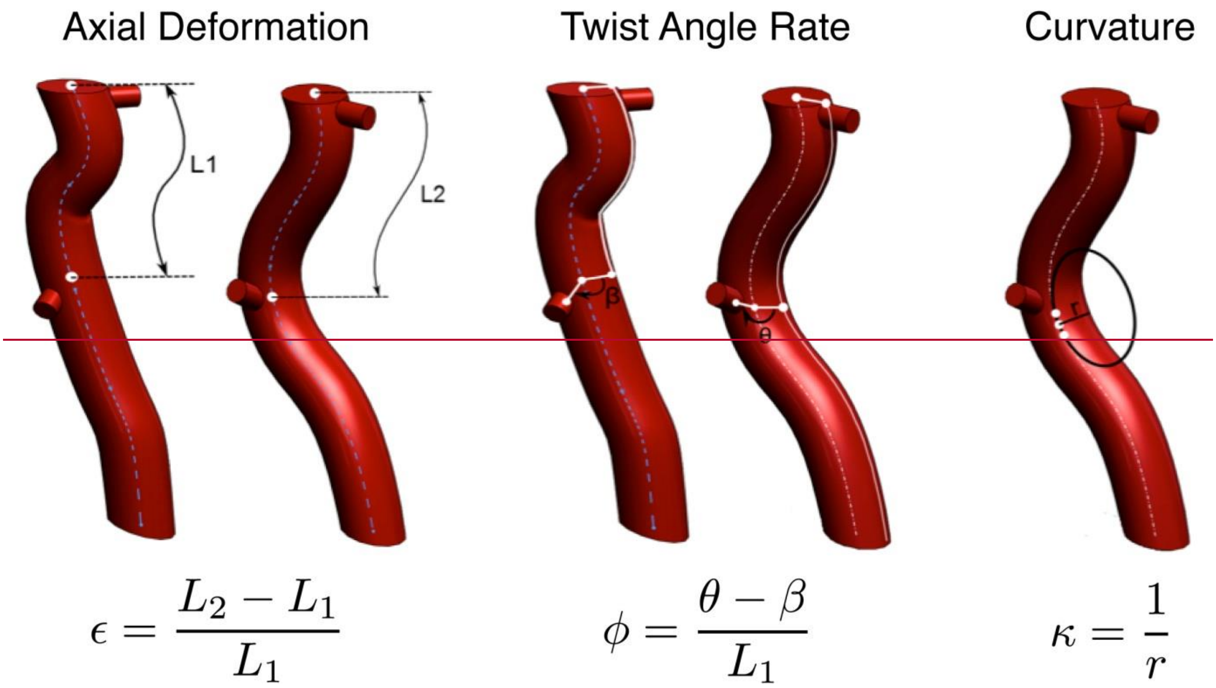




Figure 3: Quantification of deformations on the artery: For axial elongation (left), the difference in length of the centerline between the identified landmarks was measured; for torsion (middle), the change in orientation of arterial branches was calculated; and for curvature (right), the inverse of the radius of the circle, defined by three points on the centerline, was calculated.

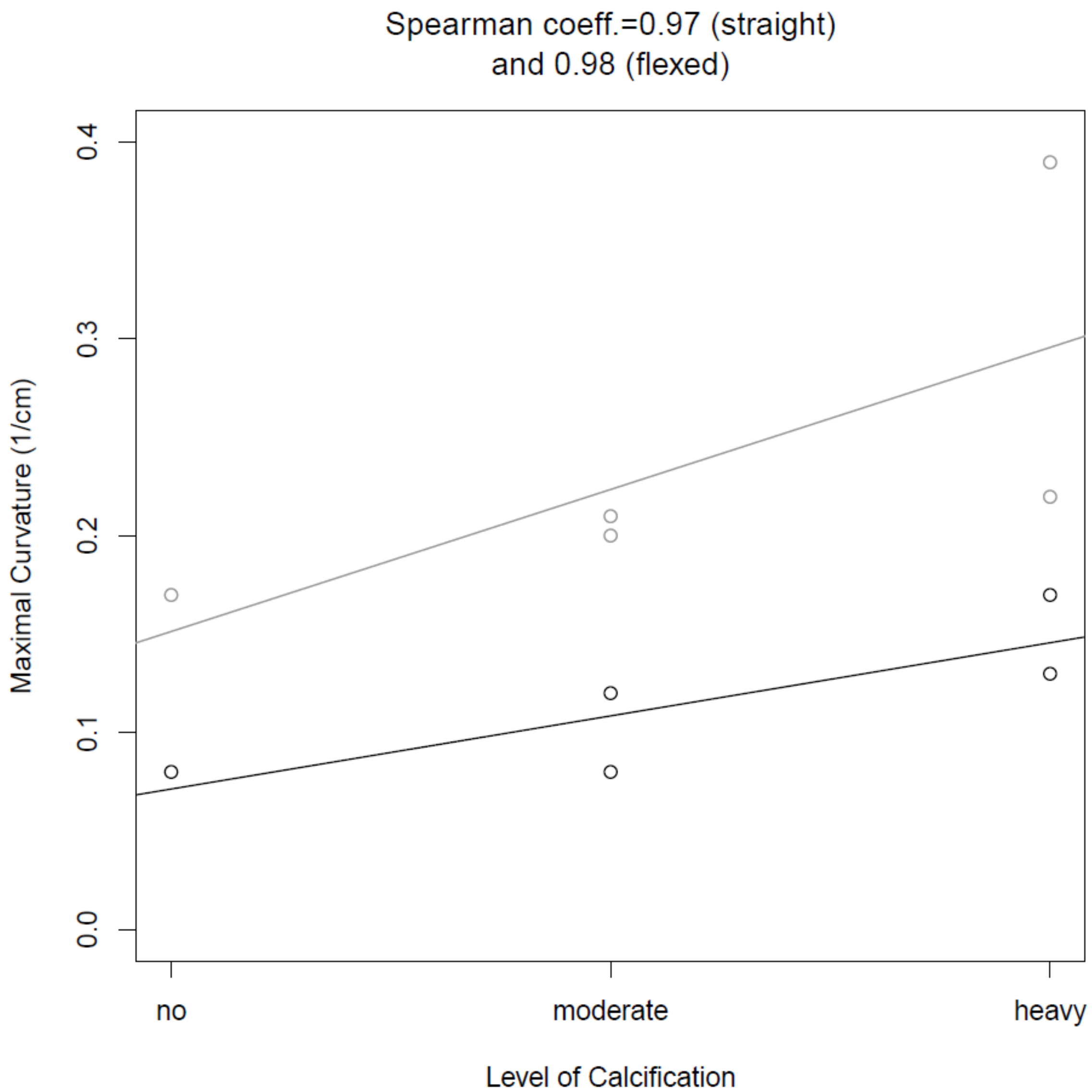



Figure 4: Deformation behaviors of the popliteal arterial segments of five patients with respect to different calcification levels for a ~~)~~ maximal curvatures ($cm^{-1}$) in straight (~~gray~~black) and flexed (gray~~black~~) legs. Vascular calcification was assessed using a semi-quantitative scoring system: no (0), moderate (1) and heavy (2) calcification.