# Roentgen stereophotogrammetric analysis to study dynamics and migration of stent grafts

Koning, O.H.J.

CHAPTER

5

# Roentgen Stereophotogrammetric Analysis to detect and quantify stentgraft migration in an animal model

Olivier H.J. Koning
Jan-Willem Hinnen
Eric H. Garling
Lucia J.M. Kroft
Edwin van der Linden
Jaap F. Hamming
Edward R. Valstar
and J. Hajo van Bockel

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## Abstract

**Objective:** To study detection and quantify stentgraft migration with RSA in-vivo as compared with CT and to evaluate the application and detection of a nitinol endovascular clip as an aorta reference marker for RSA.

**Design:** experimental animal model.

**Materials and Methods:** A model of a stentgraft was positioned in the thoracic aorta of two pigs. Tantalum aortic reference markers were attached to the adventitia for CT and RSA analysis. Nitinol endovascular clips (NEC) were inserted in the aortic wall for RSA analysis. Stentgraft migrations were measured with CT and RSA. CT images acquired with 64×0.5-mm beam collimation were analyzed with Vitrea postprocessing software using a standard clinical protocol and central lumen line reconstruction. RSA images were analyzed using standard Medis RSA software.

**Results:** The standard deviation of the measurements by RSA using tantalum markers was 0.33mm**.** The standard deviation of the measurements by CT with 3D reconstruction was 0.47mm. Placement of the clips was performed without difficulty or adverse effects but radiopacity of the clips was insufficient to allow detection with the RSA software.

**Conclusion:** RSA to measure stent-graft migration in vivo is feasible and very precise. Precision of RSA was superior to CT with 3D image reconstruction if a well defined aortic reference marker was applied for CT analysis. Placement of an aortic reference marker may facilitate CT surveillance for migration after EVAR. RSA has several other advantages over CT. Therefore, it may be a valuable tool for EVAR surveillance. The nitinol clip tested in this study as an aortic reference marker needs to be modified to increase radiopacity to enable RSA analysis.

## Introduction

Stentgraft migration is a potentially lethal failure after endovascular aneurysm repair (EVAR) [1]. Migration incidence increases over time and still occurs despite modifications of design in the latest generation of stentgrafts.[2-5] In a patient cohort study by Sun, comparing measurement in axial CTA images to 3D image reconstructions, stentgraft migration appeared to occur in all patients, even if supplied with strong hooks and barbs, proving that more accurate detection methods indeed show more stentgraft migration. [4] In case of aneurysm diameter reduction after EVAR, the main points of interest in surveillance are detection of stentgraft migration and stentgraft disintegration at the earliest stage.

In previous studies of experimental models, detection of stentgraft migration using Roentgen Stereophotogrammetric Analysis (RSA) has been described.[6-8] RSA proved to be very accurate and stentgraft migration could be detected with RSA with a mean error of 0.5mm.[7] RSA imaging also enables stentgraft structure evaluation.[6,7]

Compared to CT with 3D image reconstruction, advantages of RSA over CT are that RSA is a low cost test, with a radiation exposure that is only a fraction of that of CT, while intravascular contrast is not required.[6] Furthermore, RSA compared favorably to CT with 3D image reconstruction in detecting migration in experimental studies. [6,7] However, RSA has not been tested in vivo for evaluation of stentgraft migration. The influences of human size soft tissue surroundings and respiratory and cardiac action on the results of RSA have not been modeled and are an essential step in preclinical evaluation of the technique.

A disadvantage of RSA is that a reference marker is required in the aortic wall. Inserting this marker constitutes an additional procedure during the EVAR operation. A nitinol endovascular clip (NEC), designed as an endovascular stapler, has been proposed to serve this purpose, and this device has been tested successfully in an experimental model. [7]

The present study analyses the detection of stentgraft migration with RSA in in-vivo animal experiments. Furthermore, we tested the application and detection of a NEC as an aorta reference marker for RSA.

## Materials and METHODS

### Animal model with stentgraft

Two 100 Kg female pigs were used. The Institutional Review Board for animal experimentation approved the study and the animals were cared for in compliance with the national guidelines

for animal experiments. After general anesthesia, the pulse rate was kept at approximately 90 per minute. Thoraco-laparotomy was performed exposing the thoracic and infrarenal aorta. Heparine was continuously administered. A Dacron 8mm conduit (Gelsoft Plus, Vascutek, Inchinnan, UK) was attached to the infrarenal aorta as a conduit for vascular access.

A Gianturco stent (Cook, Bjaeverskov, Denmark) was placed inside the thoracic aorta (Figure 1) via endovascular technique. The thoracic aorta was chosen for placement as it has the largest available aortic diameter, resembling the human situation as much as possible. The stent could be displaced, "migrated" along the aorta by pulling on monofilament fishing wire (Spro, Vianen, The Netherlands), attached to each stent side. The cranial end of the wire was passed through the left carotid artery, the caudal end was passed through the conduit on the infrarenal aorta. For RSA analysis, markers had been added at the cranial and caudal corners of the stent prior to placement (stentgraft markers). In a clinical situation, markers used to position the EVAR device can be used for this purpose.

CT analysis of stentgraft migration requires a point of reference. There is no major vascular branch in the descending aorta available as a reference for measurement like the renal artery in human clinical practice. Therefore, a 1mm tantalum spherical marker was glued to the adventitia of the aorta with Histoacryl® (B.Braun Aesculap, Tuttlingen, Germany).

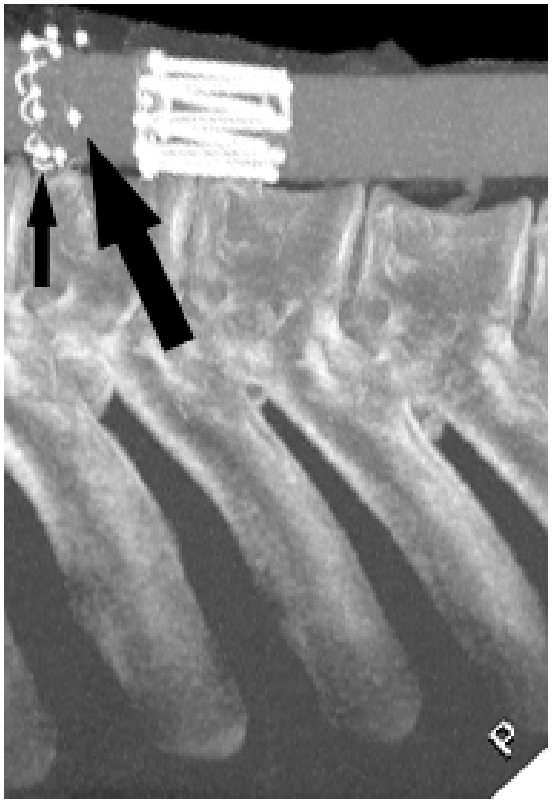

**Figure 1.** 3D maximum intensity projection of the CT image of the thoracic aorta. Small arrow lower left: nitinol clip; large arrow right: tantalum marker. Cranial side to the left.

Also for RSA analysis, reference markers were attached to the aorta, the aorta markers. We tested two sets of aorta markers: a cluster of 8 tantalum markers (with a diameter of 1 mm), glued to the adventitia with Histoacryl®, representing the standard clinical RSA situation as used to detect micromotion after joint replacement surgery (Figure 1); and three Anson Refix® Nitinol endovascular clips (Lombard Medical, Didcot, United Kingdom) (Figure 1 and 2) placed in the aortic wall by endovascular technique, to represent a clinical endovascular application.
In the first animal, two stentgraft positions were analyzed: the initial or reference position and one migration. In the second animal, five stentgraft positions were analyzed: the initial or reference position and four migrations.



**Figure 2.** Nitinol endovascular clip.

For each stent-graft position CT and RSA imaging was performed. The stent-graft was migrated caudally under visual control with an image intensifier (Philips BV300 plus, Philips Medical Systems Europe, The Netherlands).
The animals were sacrificed after the experiments and autopsy was performed to study the position of the clips and local adverse effects of the clip placement.

## RSA imaging technique

Roentgen Stereophotogrammetric Analysis (RSA) is comparable to stereo vision of human eye sight. By comparing two calibrated simultaneous images taken at a different angle, the position of an object in space can be determined. It is based on calculating 3-dimensional coordinates of radiopaque markers in the body using a stereo image of these markers. [6,9] A calibration box is positioned between the patient and the X-ray films, to define a 3-D laboratory coordinate system.[6] We used two manually synchronized standard mobile Roentgen tubes (Philips Practix 2000, Philips Medical Systems Europe, The Netherlands). The exposure settings used were: 125 kV/15mAs, resulting in an exposure time of 160msec for all RSA images.

The image postprocessing was done on a personal computer with the help of special RSA software[9-11] (Model Based RSA software, MEDIS Specials BV, Leiden, The Netherlands) after digitizing the films.[6] The RSA images were randomly numbered and the reviewer was blinded for the distance of migration induced.

Using RSA, it is possible to calculate the distance between two (groups of) markers inside the body. Migration is determined by comparing an initial, reference RSA image to the follow up RSA image. The technique was described in more detail in previous studies.[6,7]

In RSA analysis, the relative positions of markers do not change in absence of migration. Any change in relative position indicates movement between the markers. Positioning of the animal, or the patient in clinical practice, is not critical as the calibration box will facilitate the calculation of marker coordinates each time an RSA image is taken.

Pulsatile motion of the aorta may influence measurement, as each RSA image is acquired at a random point in the cardiac cycle. To study the in-vivo situation and the influence of pulsatile motion on migration measurement by RSA, 5 RSA images were acquired of the reference position and 9 images of each stentgraft position after migration. The RSA images were acquired at a random point in the cycle of pulsatile circulation. Migration was assessed using cross-table analysis, comparing each of the 5 reference images to all 9 follow-up images. This resulted in 45 measurements per migration, resembling the 45 possible clinical combinations of RSA images. The measurements were performed using tantalum markers as well as NEC-s. The Nitinol endovascular clips were evaluated for feasibility as an aorta reference marker and for applicability.

To summarize the RSA results, we pooled the data to determine the variance of the method. This was done by calculating the average migration per group of 45 measurements. Afterwards, this value was subtracted from every single measurement in the same group, thereby calculating a variance from the mean value. This enabled calculation of the standard deviation and range of deviation of all RSA measurements (n=225).

## Computer Tomography (CT)

CT analysis of stentgraft migration was performed using the same technique for post-processing and analysis to measure stentgraft position is used for CT follow up in our clinical setting. Instead of using the orifice of the renal artery as a point of reference, we used a tantalum marker fixed to the adventitia of the thoracic aorta.

The CT images were acquired with a 64 detector row CT scanner, Toshiba Aquilion (Toshiba Medical Systems, Otawara, Japan). Scanning parameters were: 100 kV, 350 mA, 500-ms rotation,

pitch factor 0.83, 0.5-mm beam collimation. The images were reconstructed with a 0.5-mm thickness and 0.4-mm reconstruction interval.

The CT images were enhanced with Iomeprol 816.5 mg/ml intravascular contrast (Iomeron 400, Altana Pharma, Hoofddorp, The Netherlands) to obtain an enhancement level of 250 Hounsfield units in the aorta for each CT image acquisition.

A reference CT scan was made of the initial stentgraft position. After each stentgraft migration, imaging was repeated. The CT images were randomly numbered and the observers were blinded for the amount of migration induced.

Using Vitrea2 post-processing software (Vital Images Inc., Plymouth, MN, USA), stentgraft migration was measured on 3D curved multiplanar reconstructions along the aortic central lumen line to evaluate the aorta in 2 perpendicular longitudinal directions as well as the perpendicular axial direction. Using automatic calipers, the distance was measured between the tantalum aorta reference marker and the stent at the level where the first circumferential view of the stent was observed (in perpendicular axial direction). The stent struts were used for orientation.

CT requires interpretation by an observer, and subsequently involves possible human error and inter-observer variability. To correct for inter-observer variability, CT scans were evaluated by five medical specialists; four radiologists and a vascular surgeon, all experienced users of this technique. Migration was determined by comparing the distance between the aortic reference marker and the stentgraft in the follow up CT to the distance in the reference CT image, as measured by the same observer.

To summarize the CT results, we pooled the data to determine the variance of the modality. This was done by calculating the average migration per group of 5 measurements. Afterwards, this value was subtracted from every single measurement in the group of five, thereby calculating a variance from the mean value. This enabled calculation of the standard deviation and range of deviation of all CT measurements (n=25).

## Results

### Nitinol endovascular clip

The application of the NEC was performed without difficulty or complications in both animals. The clips could be positioned and repositioned without failure of device and introducer. Visibility of the NEC with the image intensifier was good. Autopsy revealed no local adverse effects,

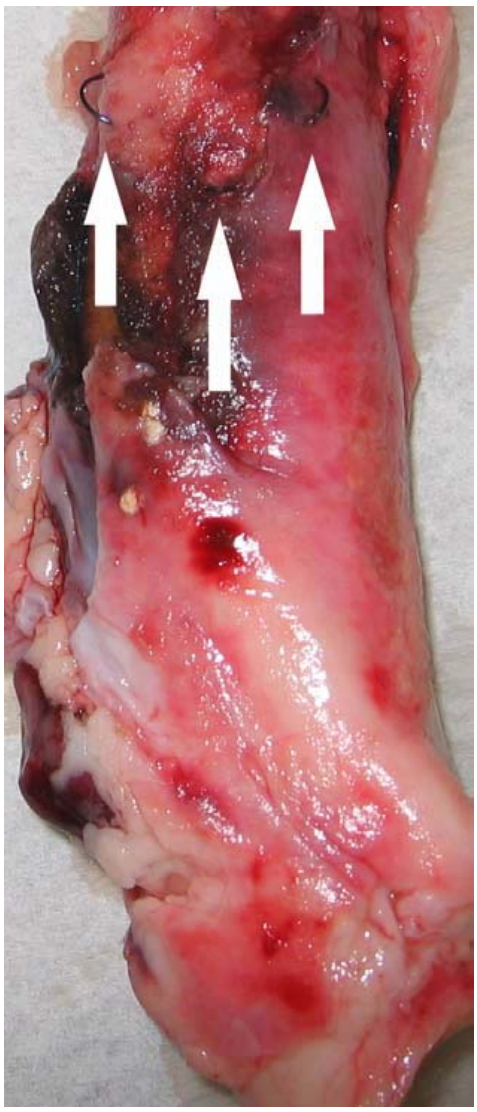

**Figure 3.** Specimen of the thoracic aorta. The wall of the aorta is (intentionally) perforated by the clip (arrows). No adverse effects were noted locally.

specifically no evidence of haematoma or perforation other than the intended perforation of the aortic wall by the anchors of the NEC (Figure 3).

However, the NEC had insufficient radiopacity to enable analysis of the stereo images with RSA in large animals of 100 kg. Therefore, the marker position could not be determined accurately using the software.

## RSA measurements

RSA measurement of stentgraft migration with the tantalum aorta reference markers was possible in all cases. The results of the RSA measurements of stentgraft migration are shown in Figure 4. The standard deviation of the measurements by RSA was 0.33mm (range -1.35

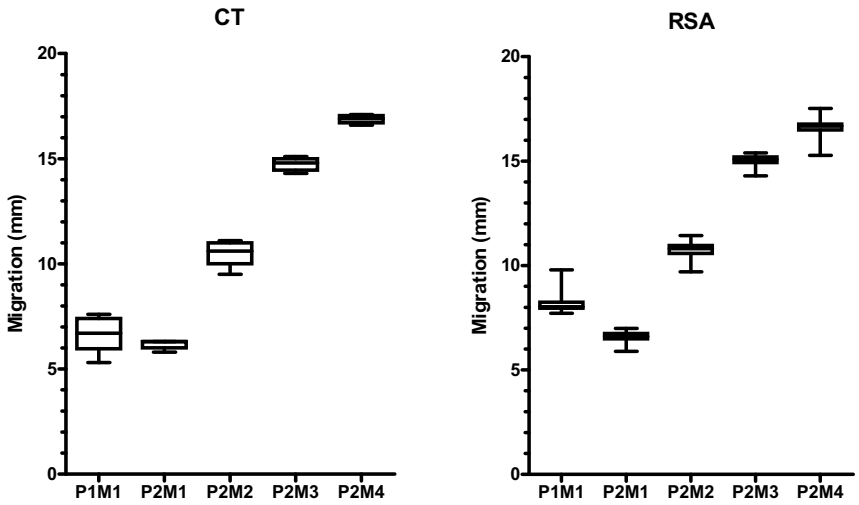


**Figure 4.** Results of the measurements with RSA and CT with 3D image reconstructions using a tantalum marker as a reference point (see figure 1). X-axis: P1M1=Pig 1, Migration 1; P2M1=Pig 2, Migration1; etc. Y-axis :migration (mm) mean, 25th and 75th percentiles and range, including all outliers.

– 1.64mm) as compared to the mean value of the corresponding group of migrations (n=225). There were five outliers with a deviation from the mean of >1 mm (2.2%).

### CT measurements

The results of the CT measurements of stentgraft migration using a tantalum aorta marker as a point of reference are shown in Figure 4. The standard deviation of the measurements by CT with 3D reconstruction was 0.47mm ( -1.38 – 0.92mm) as compared to the mean value of the corresponding group of migrations (n=25). There were two outliers with a deviation from the mean >1 mm (8%).

## Discussion

Roentgen stereophotogrammetric analysis of stentgraft migration is feasible and very precise in this in vivo animal model. This study confirms favorable results in previous in-vitro work. Despite soft tissue surroundings and the pulsatile change that occurred due to cardiac action, the variation in measurement is very low (SD = 0.36mm). Unfortunately, the nitinol endovascular clip did not have sufficient radiopacity to allow detection by RSA software.

Five outliers with a deviation of more than 1 mm from the mean were identified in 225 measurements (2%). We analyzed the outliers and found that these were due to the fact that the software had problems in identifying the markers on the cranial side of the stent due position symmetry of the markers. The circular position (see figure 1) diminishes the ability

of the software to recognize the 9 identical markers based on the stereo image, in which they projected in one row. An asymmetrical distribution of markers on the stent will solve this problem. The currently marketed stentgrafts either have this asymmetrical distribution (e.g. Zenith, Cook) or have less and therefore easier distinguishable markers (e.i. Excluder, Gore and Talent, Medtronic). Furthermore, automated pattern recognition of the stent could enable RSA data analysis regardless of marker position. This is subject to further study at our institution.

The reproducibility of CT with 3D image reconstruction (SD=0.47) was slightly less than RSA. This compared favorably to a previous study comparing 3D-CT to RSA in a pulsatile in vitro model.[7] In this model, a renal artery was used as a reference. As expected, it appears that the accuracy of the CT measurements increases by using a better defined reference point like a tantalum marker as compared with the less defined renal artery. Thus, adding a marker to the aortic wall as a reference point for CT analysis facilitates highly accurate migration detection with CT analysis using 3D image reconstruction, and this result is achieved without the use of intravascular contrast. 3D image reconstruction is a powerful tool to detect stentgraft migration and has shown better results in migration detection than reviewing axial images only, as is current practice in many centers world wide.[4] Furthermore, the cost of routine post-EVAR surveillance using CT will remain high, although radiation dose could possibly be diminished to that of a low dose CT image. Because of these considerations, we believe that RSA could be preferable over CT for routine surveillance in patients with a decreased aneurysm size after EVAR.

When considering our animal model, this experiment represents a step closer to clinical applicability. The study clearly shows feasibility of RSA under physiological in-vivo conditions. However, the consistency of the aorta of the pig is different from an atherosclerotic aneurysm neck. This may have impact on NEC placement in the bare aortic wall. During placement, the visibility of the marker using the image intensifier was good. As stated, the NEC could not be detected by the RSA software due to insufficient radiopacity of these markers in moderate low contrast resolution projection imaging techniques. Because a stereo image is produced for RSA, scatter

**Figure 5.** Platinum ring attached to the nitinol endovascular clip for enhanced radiopacity.

radiation may further decrease image contrast and visibility of the marker. In order to enable RSA analysis using the NEC as a reference marker, the radiopacity of the marker should be enhanced. This could be achieved by adding radiopaque metal to the clip, for instance a small gold or platinum ring (Figure 5). Recent preliminary studies at our institution into this issue are encouraging. Digital flat panel Roentgen detectors instead of analogue films will also enhance marker visibility. The design and safety of the marker are subject to further study at our institution.

### Conclusion

RSA to measure stent-graft migration in vivo is feasible and very precise. Precision of RSA was superior to CT with 3D image reconstruction if a well defined aortic reference marker was applied for CT analysis. Placement of an aortic reference marker facilitates CT surveillance for migration after EVAR. Because RSA has several other advantages over CT, it may be a valuable tool for EVAR surveillance. The nitinol clip, tested in this study as an aortic reference marker, needs to be modified to increase radiopacity to enable RSA analysis.



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