Left and right ventricular lead positions are imprecisely determined by fluoroscopy in cardiac resynchronization therapy: a comparison with cardiac computed tomography

Anders Sommer*, Mads Brix Kronborg, Bjarne Linde Nørgaard, Christian Gerdes, Peter Thomas Mortensen, and Jens Cosedis Nielsen

Aims
Fluoroscopy is the routine method for localizing left ventricular (LV) and right ventricular (RV) lead positions in cardiac resynchronization therapy (CRT). However, the ability of fluoroscopy to determine lead positions in a standard ventricular segmentation is unknown. We aimed to evaluate the accuracy and reproducibility of fluoroscopy to determine LV and RV lead positions in CRT when compared with cardiac computed tomography (CT).

Methods and results
Fifty-nine patients undergoing CRT were included. Bi-plane fluoroscopy and cardiac CT were evaluated in all patients. Pacing lead positions were assessed in a standard LV 16-segment model and in a simplistic RV 8-segment model. Four patients with LV lead displacement were excluded from the agreement analysis of LV lead position. Agreement of LV lead position between fluoroscopy and cardiac CT was observed in 19 (35%) patients with fluoroscopy demonstrating a 1-segment and ≥2-segment error in 30 (55%) and 6 (11%) patients, respectively. Agreement of RV lead position was found in 13 (22%) patients with fluoroscopy showing a 1-segment and ≥2-segment error in 28 (47%) and 18 (31%) patients, respectively. The interobserver agreement on LV and RV lead positions was poor for fluoroscopy (kappa 0.20 and 0.23, respectively) and excellent for cardiac CT (kappa 0.87 and 0.85, respectively).

Conclusion
Fluoroscopy is inaccurate and modestly reproducible when assessing LV and RV lead positions in a standard ventricular segmentation when compared with cardiac CT. Cardiac CT should be applied to determine the exact pacing site in future research evaluating the optimal pacing lead position in CRT.

Keywords
Cardiac resynchronization therapy • Fluoroscopy • Cardiac computed tomography • Left ventricular lead position • Right ventricular lead position

Introduction
Cardiac resynchronization therapy (CRT) is an established treatment in heart failure patients with left ventricular (LV) systolic dysfunction and intraventricular conduction delay who remain symptomatic despite optimal medical therapy. However, a large proportion of patients do not experience a beneficial response to this pacing strategy. Consequently, extensive research has been conducted to identify predictors of a favourable clinical outcome. Several studies have demonstrated the LV pacing site to be an important determinant of response to CRT. On the other hand, the optimal right ventricular (RV) lead position in CRT remains controversial. Bi-plane procedural fluoroscopy is used as the routine method for evaluation of LV and RV lead positions in CRT. However, the ability of fluoroscopy to correctly localize LV and RV leads in a standardized ventricular segmentation is unknown. Multidetector computed tomography (CT) produces imaging data that are isotropic, hence data can be shown in three dimensions and any two-dimensional imaging plane might be reconstructed. The datasets

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What’s new?
- Fluoroscopy is inaccurate and modestly reproducible when assessing both left and right ventricular pacing lead positions in a standard ventricular segmentation when compared with cardiac computed tomography (CT).
- Cardiac CT should be applied to determine the exact pacing site in future research evaluating the optimal pacing lead position in cardiac resynchronization therapy.

provided by cardiac CT may be more appropriate than traditional bi-plane fluoroscopy for assessment of pacing lead positions. Thus, the aims of the present study were (i) to evaluate the accuracy of fluoroscopy in describing LV and RV lead positions in CRT when compared with dedicated cardiac CT and (ii) to compare the reproducibility of fluoroscopy and cardiac CT when assessing LV and RV lead positions.

Methods

Patients

Between April 2011 and May 2012, we prospectively included 59 patients with chronic heart failure receiving a CRT pacemaker or a CRT-implantable cardioverter defibrillator at a tertiary referral centre (Department of Cardiology, Aarhus University Hospital, Skejby).

All patients had depressed LV ejection fraction (EF) (<35%), were in New York Heart Association functional Classes II–IV, and a surface electrocardiogram (ECG) with QRS duration >120 ms and left bundle branch block configuration. Patients with recent myocardial infarction (<3 months), who were pregnant or lactating, or with severe renal dysfunction (estimated glomerular filtration rate <30 mL/min) were excluded.

All patients underwent successful transvenous lead placement using commercially available leads and devices. Only active fixation RV leads were used. No LV or RV lead repositioning was performed between the implant procedure and cardiac CT. The patients were enrolled in a randomized study investigating the clinical impact of imaging-guided LV lead placement in CRT. Cardiac CT was performed as part of the study protocol.

Left ventricular function was assessed prior to CRT implant and at 6 months follow-up using echocardiographic standard apical 4- and 2-chamber views (Vivid E9, GE Medical Systems). LV EF, end-diastolic, and end-systolic volumes were estimated using Simpson’s biplane method.

All patients gave informed written consent before the implant procedure. The Central Denmark regional committee on health research ethics and the Danish Data Protection Agency approved the study.

Cardiac computed tomography acquisition and analysis

Cardiac CT was performed 6 months after CRT implantation using a second-generation dual-source CT scanner (Siemens Somatom Definition Flash, Siemens Healthcare). Computed tomography scanner settings and protocol were as previously described. During breath hold a contrast-enhanced (Optiray® 350 mg/mL, Covidien) helical retrospective ECG-gated scan timed according to contrast filling of both the RV and LV cavities was performed. An iterative reconstruction algorithm was applied (SAFIRE, Siemens Healthcare, Erlangen, Germany). The median (25th, 75th percentile) estimated radiation dose was 4.9 (3.7, 5.9) mSv. Using multiplanar and three-dimensional reconstructions, two experienced cardiologists independently determined LV and RV lead positions in the short-axis and the long-axis. In case of disagreement, the reviewers determined the lead positions by consensus. One observer reanalysed all images to evaluate intraobserver agreement. Commercially available software (Impax version 6.3, AGFA Healthcare) was used for image analysis.

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Displacement of the left ventricular lead during follow-up

To evaluate LV lead tip displacement inside the relevant coronary sinus branch at 6 months follow-up, we measured the mid-diastolic difference in perpendicular distance from the lead tip to the lead in the coronary sinus between the post-implant fluoroscopic RAO projection and cardiac CT images. Using cardiac CT, the distance was assessed in a volume rendered three-dimensional reconstruction viewed in the same RAO projection as fluoroscopy with windows settings adjusted to optimal visualization of the LV pacing lead (Figure 2). Four patients demonstrated a macroscopically visible LV lead displacement between fluoroscopy and cardiac CT. These patients were excluded from the agreement analysis between fluoroscopy and cardiac CT of assessing LV lead position. This was done to compare the imaging methods only in patients without significant LV lead displacement between the procedural fluoroscopy and follow-up cardiac CT.

Statistical analysis

Continuous variables are presented as mean ± SD and compared using unpaired and paired Student t-tests. Proportions were compared by a two-sample test of proportions. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the ability of fluoroscopy to correctly classify lead positions between the two categories of binary variables. Kappa statistics and intra-class correlation coefficients (ICCs) were computed to assess intra- and interobserver agreement for categorical and continuous variables, respectively. Kappa and ICC values <0.40 were considered poor agreement, 0.40–0.75 as fair to good agreement, and >0.75 as excellent agreement. The Bland–Altman method was applied for interobserver agreement analysis of fluoroscopy and cardiac CT to determine the LV lead position in the LV short-axis circumference and long-axis. Interobserver differences within the 95% prediction interval are referred to as within the limits of agreement. Values of $P < 0.05$ were considered statistically significant. Commercially available software (Stata version 12, StataCorp, College Station) was used for statistical analysis.

Results

Study population

Baseline characteristics of the 59 patients are presented in Table 1. All patients received optimal medical therapy, including β-blockers, angiotensin-converting enzyme inhibitor or angiotensin receptor blockers, spironolactone, and diuretics at maximum-tolerated dosages.

A significant increase in LV EF and a reduction in LV volumes were observed at follow-up (Table 1).

Assessment of left ventricular lead position

The LV lead positions were distributed across six and seven myocardial segments when assessed by fluoroscopy and cardiac CT, respectively (Figure 1). Overall agreement of segments between the two imaging modalities was observed in 19 patients (35%). Using cardiac CT as the gold standard for evaluation of LV lead position, fluoroscopy demonstrated a 1-segment and ≥2-segment error in 30 (55) and 6 (11%) patients, respectively (Figure 3). The inferior and inferolateral segments demonstrated the largest disagreement between the two imaging modalities (Table 2). Agreement of segments in case of large or small reverse LV remodelling (outside or between the 25th and 75th percentiles of change in LV end-systolic volume, respectively) after CRT was observed in 9 (33) and 10 (36%) patients, respectively ($P = 0.85$).

Among patients with a basal/mid-LV lead position, fluoroscopy misclassified six (11%) of the leads as in the apical region [sensitivity 89% (95% confidence interval (CI) 77–96%), specificity 50% (CI 1–99%), PPV 98% (CI 89–100%), NPV 14 (CI 0–58%)]. In patients with a basal/mid-LV anterolateral or inferolateral lead...
position, fluoroscopy misclassified nine (18%) of the leads as outside this region [sensitivity 82 (CI 69–91%), specificity 20 (CI 1–72%), PPV 91 (CI 79–98%), NPV 10 (CI 0–45%)].

In the LV short-axis 360° circumference, the mean LV lead position was 111 ± 26 by fluoroscopy and 133 ± 27 by cardiac CT (P < 0.0001). In the LV long-axis, the mean LV lead position was located at 46 ± 18 and 32 ± 19% of the LV length by fluoroscopy and cardiac CT, respectively (P = 0.0001).

**Displacement of the left ventricular lead during follow-up**

We found no significant difference in the perpendicular distance from the LV lead tip to the lead in the coronary sinus between the post-implant fluoroscopy and 6 months cardiac CT (0.7 ± 11 mm; P = 0.84).

**Assessment of right ventricular lead position**

The RV lead positions were distributed over eight and four RV segments when assessed by fluoroscopy and cardiac CT, respectively (Figure 1). In the RV eight-segment model, agreement of segments between fluoroscopy and cardiac CT was found in 13 (22%) patients. Using cardiac CT as the gold standard, fluoroscopy demonstrated a 1-segment and ≥2-segment error in 28 (47) and 18 (31%) patients, respectively (Figure 4). All mid-RV free wall lead positions were fluoroscopically misclassified as anterior high or mid septum. A CT verified free wall RV lead position was fluoroscopically misclassified as the septum in 21 (75%) patients [sensitivity 25 (CI 11–45%), specificity 74 (CI 55–88%), PPV 47 (CI 21–73%), NPV 52 (CI 37–68%)]. In patients with an apical RV lead position fluoroscopy misclassified

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**Table 1**  Patient characteristics

<table>
<thead>
<tr>
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<th>Value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>69 ± 9</td>
</tr>
<tr>
<td>Female</td>
<td>16 (27)</td>
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<tr>
<td>Ischaemic cardiomyopathy</td>
<td>31 (53)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>13 (22)</td>
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<tr>
<td>Arterial hypertension</td>
<td>10 (17)</td>
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<tr>
<td>NYHA functional Class II/III/IV</td>
<td>29 (49)/27 (46)/3 (5)</td>
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**Medical therapy**

- β-blockers: 53 (90)
- ACEI/ARB-II: 54 (92)
- Diuretics: 42 (71)
- Spironolactone: 29 (49)
- QRS width (ms): 163 ± 22
- Pre-implant LV end-diastolic volume (mL): 256 ± 72
- Pre-implant LV end-systolic volume (mL): 195 ± 58
- Pre-implant LV EF (%): 24 ± 6
- Pre-implant creatinine (μmol/L): 98 ± 31
- Pre-implant estimated glomerular filtration rate (mL/min): 66 ± 19

**Follow-up LV lead positions**

- Received a CRT-implantable cardioverter defibrillator: 40 (68)
- Follow-up LV end-diastolic volume (mL): 204 ± 76
- Follow-up LV end-systolic volume (mL): 135 ± 66
- Follow-up LV EF (%): 36 ± 11

Values are expressed as mean ± SD or n (%). ACEI/ARB-II, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers II; CRT, cardiac resynchronization therapy; EF, ejection fraction; LV, left ventricular; NYHA, New York Heart Association.

*P < 0.0001 vs. pre-implant value.

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**Figure 3**  Examples of both disagreement (A) and agreement (B) between fluoroscopy (top) and cardiac CT (bottom) on the LV lead tip position (arrow). (A) Fluoroscopy showing a lateral LV lead position in the basal portion of the LV. Cardiac CT reveals a LV lead position in the posterior basal segment. (B) Fluoroscopy and cardiac CT are both showing a posterior mid-LV LV lead position. *right ventricular (RV) lead; LAO, left anterior oblique; RAO, right anterior oblique.
28 (61%) of the leads as basal/mid-RV [sensitivity 39 (CI 25–55%), specificity 100 (CI 75–100%), PPV 100 (CI 81–100%), NPV 32 (CI 18–48%)].

Reproducibility

Table 3 shows the intra- and interobserver agreements for fluoroscopy and cardiac CT when evaluating segmental and regional LV and RV lead positions.

In the LV short-axis 360° circumference, the ICC within observers was 0.74 (CI 0.59–0.84) and 0.94 (CI 0.90–0.96), while between observers it was 0.68 (CI 0.50–0.80) and 0.88 (CI 0.81–0.93) for fluoroscopy and cardiac CT, respectively. In the long-axis, the ICC within observers was 0.79 (CI 0.67–0.87) and 0.99 (CI 0.98–0.99), while between observers it was 0.61 (CI 0.42–0.75) and 0.97 (CI 0.95–0.98) for fluoroscopy and cardiac CT, respectively. Cardiac CT had the narrowest limits of agreement between observers in both cardiac planes (Figure 5).

Discussion

The present study demonstrates that bi-plane fluoroscopy is inaccurate for localizing LV and RV pacing lead positions when compared with cardiac CT. Both intra- and interobserver agreements for assessing LV and RV lead positions were modest for fluoroscopy when compared with an excellent reproducibility for cardiac CT.

The LV pacing site is an important predictor of a favourable outcome in patients undergoing CRT. Routinely, fluoroscopy has been applied for assessing the LV lead position according to a standardized LV segmentation in studies investigating the clinical impact of different LV pacing sites. A recent report showed...
fluoroscopy to be imprecise for assessing the LV lead position when compared with thoracic CT. In the latter study, however, there were several limitations, e.g. the use of non-gated CT scans without optimal contrast enhancement, applying a non-standardized LV myocardial segmentation, and a single operators interpretation of intra-procedural fluoroscopic images for determination of LV lead location, respectively. Using cardiac CT with contrast enhancement optimized for localizing pacing lead position as the gold standard, we found fluoroscopy inaccurate for determining LV lead position on single segments in a standard LV 16-segment model. Fluoroscopy misclassified LV lead positions anterolateral and apical, respectively. Misclassifying pacing lead position may

| Table 3 | Intra- and interobserver agreement for fluoroscopy and cardiac CT when evaluating segmental and regional LV and RV lead positions |
|---|---|---|---|---|
| | Intraobserver agreement | Interobserver agreement |
| | Fluoroscopy | Cardiac CT | Fluoroscopy | Cardiac CT |
| LV lead position | | | | |
| 16-segment model | 0.42 (0.25–0.53) | 0.91 (0.88–0.96) | 0.20 (0.10–0.27) | 0.87 (0.84–0.92) |
| Basal/mid vs. apical region | 0.40 (0.09–0.70) | 1.00 (1.00–1.00) | 0.00 (−0.25–0.24) | 1.00 (1.00–1.00) |
| Basal/mid posterior–lateral vs. other region | 0.31 (0.03–0.71) | 1.00 (1.00–1.00) | 0.06 (−0.21–0.33) | 0.93 (0.80–1.00) |
| RV lead position | | | | |
| Eight-segment model | 0.37 (0.27–0.43) | 0.88 (0.81–0.90) | 0.23 (0.15–0.29) | 0.85 (0.78–0.92) |
| Basal/mid vs. apical region | 0.55 (0.32–0.79) | 0.82 (0.65–0.99) | 0.50 (0.26–0.75) | 0.77 (0.58–0.96) |
| Septum vs. free wall | 0.15 (−0.08–0.38) | 0.97 (0.90–1.00) | 0.17 (−0.08–0.41) | 0.97 (0.94–1.00) |

Values are kappa (95% CI). CT, computed tomography; LV, left ventricular; RV, right ventricular.
underestimate the effect of optimal LV lead placement on the CRT outcome. Accordingly, using a standard LV segmentation cardiac CT should be considered to determine the exact LV pacing site in future research on the clinical impact of LV lead position. In clinical practice, a post-implant cardiac CT may be performed in patients not responding to CRT to confirm the exact lead position and assess the presence and location of additional cardiac veins before considering LV lead revision. In addition, a pre-implant threedimensional visualization of cardiac venous anatomy by cardiac CT may be combined with other imaging modalities for procedural fluoroscopic transvenous targeting of an optimal LV segment.25

In the present study, fluoroscopy showed a larger agreement with cardiac CT when expanding to determine LV lead positions in larger regions combining basal and mid-LV segments or anterolateral and inferolateral segments. However, recent studies have demonstrated conflicting results of LV pacing targeted to selected single myocardial segments. When pacing concordant as compared with adjacent to an a priori selected optimal LV pacing site, both superior9 and non-superior12 clinical outcomes have been observed after CRT. These studies used fluoroscopy to determine LV lead positions. Future studies applying cardiac CT for assessing LV lead positions should be performed to clarify the clinical implications of reaching an optimal single myocardial segment for LV pacing compared with pacing adjacent or remote to an optimal segment.

In the current study, we also evaluated the displacement of the LV lead inside the coronary sinus tributary during follow-up after CRT implantation. We found no significant difference in distance from the LV lead tip to the lead in the coronary sinus between the procedural fluoroscopy and 6 months cardiac CT. Thus, displacement of the LV lead during follow-up cannot explain the observed disagreement of LV lead positions assessed by fluoroscopy and cardiac CT.

The impact of RV lead position on the clinical outcome after CRT has been investigated in retrospective and prospective studies. The results are conflicting and there is no general agreement on the optimal RV pacing site.13–16 These studies all have applied fluoroscopy to assess the RV lead position. We used cardiac CT as the gold standard to evaluate the ability of fluoroscopy in determining the RV lead position. Employing a simplistic RV 8-segment model, we found fluoroscopy to be highly inaccurate to determine the RV lead position when compared with cardiac CT. Among those with a true apical or free wall RV lead position, fluoroscopy misclassified the majority of the leads as in the basal/mid-RV region or on the septum, respectively. These findings may be important in explaining the conflicting results found in previous studies assessing the importance of RV lead position. Consequently, dedicated cardiac CT is recommended to determine the exact RV lead position in future studies evaluating the impact of different RV pacing sites on the clinical outcome after CRT.

Standard bi-plane fluoroscopy cannot account for an unpredictable positioning of the heart in the thoracic cavity, cardiac dilatation, and rotation in heart failure patients. When analysing cardiac CT images, the heart can be aligned exactly according to its long-axis and pacing lead positions can be easily determined using a standard ventricular segmentation. Accordingly, this may in part explain the observed disagreement between fluoroscopy and cardiac CT when evaluating LV and RV lead positions. To develop a fluoroscopic strategy to increase the accuracy of determining lead positions in heart failure patients, it may be necessary to use alternative projections or rotational angiography.

In prior studies, LV and RV lead positions have been determined without reporting intra- and interobserver agreements for fluoroscopy or thoracic CT.8–10,12–16,25 Assessing both LV and RV lead positions, we demonstrated a poor intra- and interobserver agreement by fluoroscopy compared with an excellent agreement within and between observers for cardiac CT. A low reproducibility of fluoroscopy increases the risk of misclassifying pacing lead position. This may contribute to underestimate the effect of optimal lead placements on the CRT outcome when evaluating lead positions by fluoroscopy. Based on the high reproducibility of cardiac CT, this imaging modality may currently be recognized as the gold standard for assessment of LV and RV lead positions.

Limitations
We acknowledge the inherent limitations of a single-centre study with a moderate sample size. Nevertheless, this is the first study evaluating the ability of fluoroscopy to determine exact LV and RV lead positions in a standardized ventricular segmentation when compared with dedicated cardiac CT.

We compared procedural fluoroscopy with cardiac CT performed 6 months after CRT implant and LV remodelling was observed during follow-up. However, the relationship between the coronary venous anatomy and the LV myocardial segments is presumably unaltered despite cardiac remodelling. Furthermore, similar agreement proportions on the segmental LV lead position were present in patients with the smallest and largest reverse LV remodelling.

In contrast to our study, others have applied electrophysiological parameters to confirm a septal RV lead position.16 However, this method has not been elucidated in heart failure patients. Furthermore, fusing fluoroscopic venous angiograms with other imaging modalities may improve the precision of fluoroscopy to validate LV lead positions.26 Still, this will require an accurate fusion algorithm.

The introduction of cardiac CT into the diagnostic algorithm in CRT patients will increase their cumulative radiation exposure. Several approaches to minimize the radiation dose are applied in this study, including the use of iterative reconstruction algorithms, individual settings of tube voltage and current, and tube current modulation with a narrow full current window, respectively.19,27

Conclusions
Fluoroscopy is inaccurate for localizing both LV and RV lead positions when compared with cardiac CT in heart failure patients undergoing CRT. Agreement of lead positions within and between observers was modest for fluoroscopy versus excellent for cardiac CT. Future studies investigating the clinical impact of LV and RV lead positions should apply cardiac CT to determine the exact ventricular pacing sites.

Conflict of interests: J.C.N. has received speakers’ honoraria from Biotronik, Biosense Webster, St. Jude Medical, and Medtronic and a research grant from Biosense Webster. P.T.M. and C.G. have received speakers’ honoraria from Biotronik. All other authors have no conflicts of interest to disclose.
Funding
This work was supported by the Danish Heart Foundation (grant number 11-04-RB4-A2334-22641) and the Danish Council for Independent Research (grant number 11-107461).

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