# An unexpected cause of a swollen pacemaker pocket: a case report

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Background	A complication originating from the pacemaker pocket after device implantation can most often be explained by a post-opera- tive pocket haematoma, or, less frequently, by a pocket infection. Both conditions need immediate assessment, dedicated treat- ment, and specialized follow-up. In rare cases, however, a swollen pacemaker pocket has an alternative diagnosis, which is exemplified by the following case.
Case summary	A 70-year-old male patient had a-specific symptoms of fatigue, dyspnoea, and coughing for some weeks. He also noted an evident, new swelling of his pacemaker pocket several months after pacemaker implantation, a procedure that was performed in a high-volume center and without any complication. Ultrasound imaging of the pocket suggested the presence of a soft tissue mass with increased vascularity, rather than a fluid collection or a late organized haematoma. Ultrasound-guided biopsy of the mass was obtained for histopathology analysis and revealed a well-differentiated invasive squamous cell carcinoma. Additional PET-CT imaging demonstrated multiple fluorodeoxyglucose-avid hotspots: a voluminous lesion in the left lung hilum, smaller lesions in the liver, some mediastinal lymph nodes, several bone lesions, and a large mass surrounding the pacemaker. The multidisciplinary oncologic specialty team concluded that the patient had an aggressive metastatic lung carcinoma. The patient refused to undergo further treatment and died 1.5 months after diagnosis.
Discussion	To the best of our knowledge, we did not find any earlier reports of a squamous cell carcinoma of the lung spreading to a pace- maker pocket. Presentation of a primary tumour or a metastasis in a pacemaker pocket is extremely rare. Ultrasound imaging with ultrasound-guided biopsy is a fast and reliable method to sample the tissue and to obtain a reliable diagnosis.
Keywords	Case report • Pocket haematoma • Pacemaker • Soft-tissue mass • Squamous cell carcinoma
ESC Curriculum	5.9 Pacemakers • 9.9 Cardiological consultations

#### Learning points

- When observing a soft-tissue mass in or around a pacemaker pocket several months after pacemaker implantation, a malignant process should be part of the differential diagnosis.
- The key to a fast and accurate diagnosis of a soft-tissue mass in or around a pacemaker pocket is ultrasound imaging and eventually ultrasound-guided tissue sampling.
- PET-CT imaging is of added value to detect the eventuality of a primary tumour and for staging of the oncologic disease.

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#### Introduction

Implantation of a cardiac implantable device is a routine procedure that should go along with careful post-operative monitoring of the device pocket in search for possible complications. Among the most frequent post-operative complications are: pocket haematoma, <sup>1</sup> pocket infection, <sup>1,2</sup> and cardiac device-related infective endocarditis (CDRIE).<sup>2</sup> Presentation of a primary tumour or a metastasis in a pacemaker pocket is rare, yet several case reports are available in the literature.<sup>3–17</sup> Reporting these rare cases is particularly relevant to understand the metastatic behaviour of tumours and their predilection for prosthetic material.

## Timeline

Day 0	Successful two-chamber pacemaker implantation
Day 1,	Normal post-operative control, correct pacemaker
day 2	function, clinically unremarkable pacemaker pocket
Day 84	Normal routine outpatient check-up with normal
	pacemaker function and clinically unremarkable pocket
Day 272	Routine outpatient check-up, patient reports no problems
	except a prominent mass in the pacemaker pocket, painless but annoying
Day 272	Ultrasound imaging of soft-tissue mass, CT imaging, reveals
	soft-tissue mass around the pacemaker, haematoma or
	infection is excluded
Day 282	Ultrasound-guided biopsy of soft-tissue mass is performed
	and sent for anatomopathological analysis
Day 289	PET-CT imaging of total body reveals active oncologic
	process in the left lung hilum, the liver, mediastinal
	lymph nodes, bone lesions and a soft tissue mass around
	the pacemaker
Day 290	Histopathological results of biopsy sample show evidence
	of a metastatic lesion of a squamous cell carcinoma
Day 302	Multidisciplinary oncological assessment concludes that
	the patient suffers from an aggressive squamous cell
	carcinoma probably originating from the lung; patient
	refuses any form of anti-cancer treatment and
	consciously opts for palliative care
Day 318	Patient deceased

## **Case description**

A 70-year-old male patient with a history of extensive nicotine abuse, laryngeal squamous cell carcinoma seven years ago, bladder urothelial carcinoma ten years ago, and a dual-chamber pacemaker (type Medtronic Azure XT W2DR01 MRI Surescan, an RV lead type Medtronic 5076 Capsure Fix Novus MRI 59 cm and an RA lead type Medtronic 5076 Capsure Fix Novus MRI 52 cm) implanted 9 months ago for sick sinus syndrome, was seen routinely in the outpatient cardiology clinic. He had complaints of persisting fatigue, dyspnoea, and coughing. He had been tested positive for COVID-19 infection three weeks earlier, but strangely his symptoms did not abate with time and were rather progressive. He also noted an evident, new swelling of his pacemaker pocket (*Figure 1A* and *B*). At the outpatient clinic, the patient had normal blood pressure, normal heart rate, no signs of cardiac decompensation or cachexia. Chest ultrasound suggested the presence of a soft tissue mass with increased vascularity, rather than a collection or a late haematoma (*Figure 1C* and *D*). The mass was also identified using conventional CT imaging (*Figure 2A–C*). Ultrasound-guided biopsy of the mass was obtained for histopathology and revealed a well differentiated invasive squamous cell carcinoma (*Figure 3A–C*). Additional PD-L1 staining was moderately positive (*Figure 3D*). PET-CT scan demonstrated FDG-avid lesions in the left lung hilum (*Figure 2B–D*, *arrowhead*) with multiple FDG-avid lesions present in the liver, as well as mediastinal lymph nodes and bone lesions. Furthermore, several soft tissue masses, among which a large mass surrounding the pacemaker pocket, were identified (*Figure 2*).

The patient was subsequently referred for an oncologic assessment, but he refused to undergo further treatment and chose for palliative care. He died 1.5 months after his cardiology outpatient consultation where the mass was first noticed.

#### Discussion

To the best of our knowledge, we did not find any earlier reports of a squamous cell carcinoma of the lung metastasizing to a pacemaker pocket. Based on the tissue sampling and the PET-CT images, the multidisciplinary oncology team decided that the most likely primary origin of the metastasis was the tumour in the left lung. There are case reports and small case series describing metastatic lesions of melanoma,<sup>3</sup> malignant lesions in the proximity of breast carcinoma,<sup>4–6</sup> sarcoma,<sup>7,8</sup> rhabdomyosarcoma,<sup>9</sup> cutaneous leiomyosarcoma,<sup>10</sup> squamous cell and basocellular carcinoma of the skin,<sup>11,12</sup> non-Hodgkin lymphoma,<sup>13</sup> plasmablastic lymphoma,<sup>14</sup> plasmacytoma,<sup>15</sup> and multiple myeloma.<sup>16</sup>

The detection of an active oncologic process, a primary tumour or a metastasis in a pacemaker pocket is a rare phenomenon. Depending on the time frame, after implantation of the device, primary causes of pocket swelling are pocket haematoma, inflammatory fluid collection, and pocket infection. A rare presentation of a merely local pocket infection with important fluid collection but without systemic inflammation has been described.<sup>17</sup> In the first place, ultrasound imaging of the swelling is the best tool to differentiate a soft-tissue mass from a blood collection. Whenever a soft-tissue mass is identified, an ultrasound-guided biopsy is a fast and reliable method to sample the tissue and a fast route towards a definite diagnosis. The result of the histopathology will then guide the oncologic staging process and the best additional examinations to be performed. In Figure 4, we propose a comprehensive diagnostic work up, but additional or different tests might be necessary based on the identification and characterization of the primary tumour.

Based on other case reports,<sup>5,16</sup> the time frame between implantation of the device and occurrence of a tumour metastasis in this case, is rather short: in these other reports<sup>5,16</sup> it took years for this phenomenon to take place. Another interesting question that remains unanswered, is precisely why this pacemaker pocket was a predilection site for early metastasis. Literature is rather scarce, however two cases of a squamous lung carcinoma spreading to sites of 'recent physical trauma' have been described.<sup>18</sup>



**Figure 1** Clinical appearance and ultrasound imaging of the pocket. (A) Anterior view of the macroscopic aspect of the swollen pocket, with patient in prone position. Remark the old, healed scar. (B) Profile view of the macroscopic aspect of the swollen pocket with the patient in supine position. (C) Colour-doppler ultrasound of the tissue mass surrounding the pacemaker. (D) Ultrasound imaging of the soft-tissue mass with a clear echogenic structure below which is the device battery.



**Figure 2** CT and PET-CT imaging of the soft-tissue mass and total body. (A) Anteroposterior CT image showing the pacemaker battery and the soft-tissue mass (arrow), and a left upper lobe tumour (arrowhead). (B) PET-CT image comparable to (A), showing the metabolically active soft-tissue mass in the pocket (arrow), the lung tumour (arrowhead) and several lesions in the liver. (C) CT image of the tissue mass surrounding the pacemaker (arrow). (D) PET-CT image of the lung tumour (arrowhead).



**Figure 3** Histopathology imaging of the soft tissue. Cylindrical biopsy of the soft tissue, with haematoxylin/eosin staining at  $20 \times (A)$ ,  $100 \times (B)$ ,  $200 \times (C)$ . PD-L1 staining at  $200 \times$  magnification is depicted in panel (D).



**Figure 4** Proposed diagnostic work-up for pocket swelling, with an important role for the time frame between implantation of the device, and the diagnosis of the swelling. A stepwise approach is proposed, with an important role for ultrasound as the first-in-line diagnostic examination.

In the last decades, there were some reports on 'oncotaxis', the phenomenon describing the propensity of certain solid-tissue tumours to spread to zones of recent surgery ('surgical oncotaxis')<sup>19</sup> or chronic inflammation ('inflammatory oncotaxis').<sup>20</sup> Furthermore, it remains elusive whether the presence of titanium or other substances constituting a pacemaker battery, might have pro-oncogenic properties. As far as titanium is concerned, *in vitro* reports<sup>21</sup> and experiments in human subjects<sup>22</sup> have shown that titanium can induce chronic low-grade inflammation, e.g. by activating tissue macrophages overexpressing TNF-alpha. Potentially, this low-grade inflammation with an altered micro-environment in the pacemaker pocket is an attractive site for metastatic tumour cells.

### Conclusions

When observing a soft-tissue mass in or around a pacemaker pocket months or years after pacemaker implantation, a malignant process should be part of the differential diagnosis. The key to a fast and accurate diagnosis is ultrasound imaging and eventually ultrasound-guided tissue sampling. PET-CT imaging is of added value to detect the eventuality of a primary tumour and for staging of the oncologic disease. Further research is warranted to understand which signals drive metastasis of an active cancer to a pacemaker pocket.

## Lead author biography



Dr. Ward Heggermont is a board certified cardiologist, specialized in chronic heart failure, and device implantations, especially cardiac resynchronization therapy. He combines his clinical activities in the OLV Hospital Aalst (Belgium) with basic and translational research at the Cardiovascular Center Aalst Katholieke (Belgium) and the Universiteit Leuven.

#### **Supplementary material**

Supplementary material is available at European Heart Journal – Case Reports online.

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**Slide sets:** A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

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