Device-detected atrial fibrillation (AF) episodes predict poor clinical outcome regardless of symptoms. Potential benefits of remote monitoring are early arrhythmia detection and patient continuous monitoring. Several studies of device remote monitoring consistently demonstrated that AF represents the most common clinical alert and that detailed information on arrhythmia onset, duration, and burden as well as on the ventricular rate may be early available for clinical evaluation. Reaction time to AF alerts was very short in all series involving either pacemakers or defibrillators and action ability of AF alerts was very high. In the Home Guide Registry, in which 1650 patients were enrolled, AF was detected in 16.3% of patients and represented 36% of all cardiovascular events during the follow-up. Timely anticoagulation introduction in asymptomatic patients may impact on the stroke rate. According to the results of repeated Monte Carlo simulations based on a real population of 166 patients, daily monitoring may reduce the 2-year stroke risk by 9–18% with an absolute reduction of 0.2–0.6%, compared with conventional inter-visit intervals of 6–12 months. In the COMPAS trial, the incidence of hospitalizations for atrial arrhythmias and related stroke was significantly higher in the control group than in the remote monitoring group. Major questions will be addressed by the ongoing IMPACT trial in which a remote monitoring guided anticoagulation strategy based on AF detection will be compared with a physician-directed standard strategy. In patients with heart failure, AF early detection combined with other indexes may help prevent hospitalizations.

Keywords
Cardiac implantable electronic devices • Implantable defibrillator • Remote monitoring • Atrial fibrillation • Stroke • Heart failure

Introduction
Expected benefits of remote monitoring in patients with cardiac implantable electronic devices (CIED) and atrial fibrillation (AF) are mainly represented by early arrhythmia detection and patient continuous monitoring. Early detection of AF may induce prompt clinical reaction aimed at preventing severe adverse events such as stroke and heart failure.1–3 Continuous monitoring allows individual tailoring of patient treatment and continuous updating of therapeutic strategy. It is well known that AF is very common in CIED patients even in those without any history before implant. Furthermore, the majority of events are asymptomatic.4 Cardiac implantable electronic devices keep detailed information about AF episodes, including number and duration, arrhythmia recurrences and burden, mean and maximum ventricular rate, and intracardiac electrogram (EGM) strips. Remote monitoring allows continuous access to stored data and alerts may be programmed for specific events. In Figure 1, remote transmission shows atrial fibrillation onset in a dual-chamber defibrillator [implantable cardioverter defibrillator (ICD)], clearly documented by high-quality intracardiac EGMs and marker channels.

Atrial fibrillation early detection
Atrial fibrillation detection by wireless Home Monitoring (HM) (Biotronik SE&Co.KG) was initially evaluated in 276 consecutive patients implanted with pacemakers with automatic daily remote monitoring capability who were followed for 12 ± 2 months.5 Twenty-nine patients experienced at least 1 day with AF. In each patient, days in which AF was recorded were classed by mode switch duration (irrespective of mode switch number) according to >6, >12, >18, and >24 h per day. Epidemiological analysis was permitted by automatic databasing. Atrial fibrillation burden differed significantly among and within individual patients, as represented in detail in Figure 2. For example, patient 22 had only 1 day of AF compared with 38 in patient 15. In patient 15, 81 of 93 days were associated with >18 h of AF (i.e. AF burden was heavy when it occurred). In contrast, patient 20 who had seven AF days but none of these exceeded 18 h duration on any single day.

In the worldwide HM database analysis,6 3 004 763 transmissions were made by 11 624 recipients of pacemakers (n = 4631), ICD (n = 6548), and combined ICD + cardiac resynchronization therapy

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(CRT-D) systems \((n = 445)\). The vast majority (86%) of events were disease related. Among them, AF was responsible for \(\geq 60\%\) of alerts in pacemakers and CRT-D devices and for \(\sim 10\%\) in dual-chamber ICD.

Early AF detection was tested in both pacemaker and ICD patients with different remote monitoring systems. Using inductive remote monitoring system in 980 pacemaker patients, the number of events reported per patient was significantly higher in the remote monitoring arm (wanded 3-monthly remote interrogation) than standard follow-up (in-office visit every 6 months and transtelephonic transmission every 2 months) (0.061 vs. 0.037 for new onset AF and 0.198 vs. 0.105 for AF lasting \(\geq 48\) h). With wireless remote monitoring, a pilot Italian single-centre study involving 166 patients (73% pacemakers; Biotronik, HM) demonstrated that 20% of patients

Figure 1  Atrial fibrillation onset in a dual-chamber ICD. From the top: atrial and ventricular marker channels, far field electrogram (EGM), atrial internal EGM, ventricular internal EGM. After the third sinus beat normally conducted to the ventricles, a premature atrial beat (arrow) induces AF.

Figure 2  Accurate depiction of quantification of AF burden, as documented by remote transmissions (detail in the text). Chart generated from central HM service centre data. From Varma et al\(^5\) modified.
had alerts for AF. Actionability of unscheduled follow-up for AF was 88%. The median reaction time to AF was advanced 148 days compared with scheduled follow-up, as it can be observed in Figure 3. Detailed reactions to AF alert are reported in Table 1. In the TRUST trial, (ICDs; Biotronik HM system), AF detection was 34.5 days earlier with remote monitoring vs. standard follow-up (5.5 vs. 40 days). In the CONNECT trial (ICDs; Medtronic CareLink system) the interval between an AF event longer than 12 h and the clinical reaction was eight times shorter with remote monitoring when compared with standard follow-up (3 vs. 24 days). In the same study, a ventricular rate during AF higher than 120 b.p.m. for at least 6 h was detected within 4 days with remote monitoring vs. 23 days with standard follow-up.

The HomeGuide study

The HomeGuide Registry was organized to estimate the effectiveness of device remote monitoring in clinical event detection and management and to analyse the associated outpatient clinic workload and impact on resource consumption. From March 2008 to September 2011, 1650 patients [27% pacemakers, 27% single-chamber ICDs, 22% dual-chamber ICDs, 24% CRT-D (Biotronik HM system)] were enrolled. During a 20 ± 13 months follow-up, 2471 major cardiovascular events were detected in 838 patients (51%), with a median of 2.0 events each: 2033 events (82%) were detected during HM sessions, 165 (7%) during in-person visits, and 273 (11%) in other circumstances. Generalized estimating equation-adjusted HM sensitivity and positive predictive value were
84.3 and 97.4%, respectively. Overall, 95% of asymptomatic and 73% of actionable events were detected during HM sessions. Median reaction time was 3 days. Among the true-positive events, 868 (36%) in 269 patients (16.3%) were represented by atrial tachyarrhythmias, of which 808 (93%) detected during HM sessions. Generalized estimating equation-adjusted HM sensitivity for atrial tachyarrhythmias was 94.2%. In Figure 4, AF and stroke incidence and HM sensitivity for atrial arrhythmia detection are represented.

Stroke reduction and heart failure

Early detection of AF and prompt patient management may theoretically prevent stroke. Clinical evidence for stroke risk reduction by remote monitoring is still awaited. The potential benefit of remote continuous monitoring on 2-year incidence of stroke was modelled by running repeated Monte Carlo simulations based on a real population of 166 patients prospectively followed daily. The results suggested that daily monitoring may reduce the 2-year stroke risk by 9 to 18% with an absolute reduction of 0.2 to 0.6%, compared with conventional inter-visit intervals of 6–12 months. In Figure 5 the estimated increment of 2-year risk of stroke without remote control for different intervals between scheduled in-hospital visits is represented. The COMPAS trial randomized 538 pacemaker patients and noted that the incidence of hospitalizations for atrial arrhythmias and related stroke was 0.073 in the control group and 0.024 in the remote monitoring group (P = 0.02), with a stroke rate of 0.033 and 0.008, respectively. However, this was not powered to test this hypothesis. In the HomeGuide Registry, in which all patients were followed remotely, stroke incidence was extremely low: cumulative rate in the whole population was 0.004 at 4 years.

Few studies have addressed the important interaction of AF and heart failure in patients implanted with CRT devices. Potential negative effects include heart failure worsening, more frequent hospitalizations, inappropriate ICD shocks, loss of CRT therapy, increased sympathetic tone, haemodynamic compromise, and thromboembolism. One large multicentre study (1193 CRT-D patients from 44 Italian centres) reported significantly higher freedom from the composite endpoint of death or heart transplantation or heart failure hospitalization in patients in sinus rhythm than in those with AF during follow-up. Pooled data analysis from two prospective, multi-centre, international, observational studies in CRT-D patients (everestT1 and HomeCARE2) demonstrated that patients with newly detected AF or a prior history of AF were more likely to develop thromboembolic events than patients without AF and prior AF history. Furthermore, among patients without prior history of AF, those with device-detected AF were significantly more at risk for thromboembolic events than those without. With regard to heart failure hospitalizations, again patients with prior history of AF and device-detected AF during study follow-up were more at risk than those without AF and prior AF history.

The ongoing randomized IMPACT trial in which a HM-guided anticoagulation strategy based on AF detection will be compared to a physician-directed standard strategy may resolve outstanding questions (projected 2718 patients, analysis in 2015). Main endpoint will be a composite endpoint of stroke, systemic embolism, and major bleeding.

Atrial fibrillation alert setting and clinical reaction planning

Remote monitoring offers a unique tool for continuous monitoring of AF in CIED patients. However, AF alert setting may be challenging in individual patients. First, there are major differences in different proprietary systems, either in alert itself setting (web based or directly in the implanted device) or in available options in terms of burden level, arrhythmia duration, internal EGM strips, and ventricular rate. Inductive systems have not automatic transmission triggers in case of AF, which may be detected only during scheduled periodic transmissions or by manual transmission in case of symptoms. On the other side, availability of daily alerts even for single short lasting episodes may increase clinic work burden, making more difficult to identify clinically meaningful alerts.

A key issue is represented by criteria to start anticoagulation, in particular at which AF episode duration and/or AF burden. The risk
of embolism, adjusted for known risk factors, has been reported as high as 3.1 times increased in patients with device-detected AF episodes longer than 1 day during the follow-up. In the TRENDS study a daily AF burden ≥5.5 h was associated with an increased risk of thromboembolic events of 2.2, while an AF burden <5.5 h did not show an incremental risk if compared with no AF burden. On the contrary, others have reported an increased risk even for episodes lasting just more than 5 min. Risk for thromboembolic events seems to be similar in paroxysmal vs. sustained AF in patients under treatment. Interaction between device data and clinical risk factors has been evaluated in a multicentre Italian trial. By combining AF study a daily AF burden ≥5.5 h was associated with an increased risk of thromboembolic events of 2.2, while an AF burden <5.5 h did not show an incremental risk if compared with no AF burden. On the contrary, others have reported an increased risk even for episodes lasting just more than 5 min. Risk for thromboembolic events seems to be similar in paroxysmal vs. sustained AF in patients under treatment.

### Conclusion

Effectiveness of CIED remote monitoring in early detecting and treating atrial fibrillation as well as in monitoring therapy effects and patient clinical status has been definitely demonstrated. Benefits in clinical outcome, including hospitalizations, thromboembolic events, heart failure, and survival are the aims of current and near-future investigations. The challenge for clinicians is to deal with the huge data entry, to define new organizational models to improve device patient management and to continuously update AF guidelines according to the great amount of data offered by new technology.

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### References