# Side Effects Occurrence in Single Lead DDD Pacing - One Year Follow-up in 250 Patients Using OLBI Atrial Stimulation

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**Summary**

*Reported side effects in single lead DDD pacing are: phrenic nerve and thoracic muscle stimulation and inconstant atrial capture as well. Aim of this study, performed jointly to the Italian clinical trial of OLBI atrial stimulation, was to identify implant and anatomic factors correlated to side effects and to collect data for future improvement of the system. In 40 Italian implant centers, 250 patients, all with advanced or complete AV block and uncompromised sinus function, a single A-V lead VDD/DDD pacing system allowing OLBI atrial stimulation was implanted. Follow-up was performed at 1 day, discharge and 1, 3, 6 and 12 months. Stability of atrial capture was assessed at each follow-up and a 24 h Holter monitoring was performed in 135 patients at 3 months. Data were also discriminated by implant site, patient sex and body mass index (BMI). Constancy of atrial capture (i.e.: >95% capture) was found correlated to body position, at 1 year 80.9% of patients in supine (best value) vs. 73.1% of patients in left decubitus (worst value), and to dipole position: 100% in very high atrium vs. 50% in lower atrium. No significant difference were found between sexes or implant site. Phrenic nerve stimulation (PNS) was detected in 15.2% of patients at discharge and in the 14.4% at 1 year. PNS always occurred at pulse amplitude higher than pacing threshold. PNS was significantly correlated only to sex or, better, to the BMI of the patient (6.7% PNS occurrence in males vs. 26.3% in females at 1 year). The BMI upper limit to which PNS was detected was 25. PNS was not significantly correlated to dipole position and implant site. Thoracic muscle stimulation never occurred during the whole follow-up. OLBI atrial stimulation seems to be the most promising approach for DDD back-up pacing in single lead VDD systems. PNS can be avoided through a careful evaluation of patient's BMI. The mid to high atrium is the best position to place the floating dipole. Unstable atrial capture still occurs in about 20% of patients and must be improved by limiting the floating condition of atrial electrodes.*

**Key words**

Single lead DDD pacing, OLBI atrial stimulation, side effects, atrial capture, phrenic nerve stimulation

## Material and Methods

The positive evolution and diffusion of single lead VDD pacing in treating advanced AV blocks with uncompromised sinus function is spurring clinical and technical investigators into the challenge to extend this simple approach to DDD pacing.

Literature reports of several attempts of DDD pacing using the same single AV leads, that were designed and currently used for VDD pacing, connected either to conventional DDD, or modified VDD pulse generators. The morphology of the stimulus used in all these attempt was the conventional square cathodic. The bipolar configuration of atrial electrodes was rarely tested, while unipolar was extensively investigated in both acute and chronic conditions [1-2].

However, all these attempts were rather discouraging since floating unipolar atrial stimulation was unable to reach 50 percent success and has run into problems on account of the three side effects peculiar of this pacing technique: inconstant atrial capture, phrenic nerve stimulation and thoracic muscles contraction.

The OLBI (OverLapping Biphasic Impulse) atrial stimulation technique, which optimizes the field or current distribution inside the atrial myocardium and reduces its spread in neighboring tissues, seems to be a

| body position | dis. | day 30 | day 90 | day 180 | day 360 |
|---|---|---|---|---|---|
| supine | 80.4 | 86.5 | 80.6 | 80.2 | 80.9 |
| left decubitus | 74.0 | 78.3 | 69.6 | 71.3 | 73.1 |
| right decubitus | 72.8 | 75.7 | 71.5 | 71.8 | 74.3 |
| sitting | 78.4 | 82.9 | 80.6 | 80.4 | 80.6 |
| lying | 80.0 | 82.9 | 79.9 | 80.8 | 80.6 |

*Table 1. Constancy of atrial capture (CAC) definded as a pacing giving 95-100% of constant and consecutive atrial capture during the entire period of observation. Percentages of patients showing CAC are given for different body positions at discarge (dis.) and follow up 1, 3, 6, 9, and 12 months after implant.*

very promising advancement in the challenge. OLBI technique employs two single unipolar pulses, with the same amplitude and duration but with opposite polarities. These pulses are simultaneously and separately issued between each of the electrodes of the atrial dipole and the case of the pacemaker (PM). This way, a strong field is induced in the atrial myocardium in the vicinity of the dipole. In the outer atrial wall, the interaction of opposing isopotential lines minimize the field strength and reduce the likelihood of phrenic nerve and thoracic muscles stimulation [3-5].

OLBI stimulation was investigated in an extensive Italian multicenter study. Particular attention was focused on factors influencing side effects (anatomical, surgical and technological) and collected data may probably help future improvement of the system. [6-10] In 40 implant centers a population of 250 patients, 150 male and 100 female, mean age of 75.1 ± 9.1 years, all with symptomatic A-V block and without evidence of sinus node dysfunction, were implanted by 95 PM Biotronik mod. DROMOS SL M7, allowing supervised OLBI pacing, and 155 PM Biotronik mod. EIKOS SLD, allowing unsupervised OLBI pacing. In all PM, the maximum programmable amplitude of each polarity of the OLBI configuration was of 4.8 V. All PM were connected to Biotronik single A-V leads mod. SL 60, with 1.0 cm atrial dipole spacing. An A-V distance of 13 cm was used in 216 patients (86.4%) and a 15 cm in the remaining 34 patients (13.6%).

All leads were implanted following the standard procedure of a single lead VDD system. Atrial dipole position was only selected in terms of P-wave minimum amplitude and stability. No atrial pacing was performed during implantation. Stability of atrial capture (CAC) and occurrence of both parasitic phrenic nerve stimulation (PNS) and thoracic muscles contraction were assessed at: discharge (~1 week), 1, 3, 6 and 12 months after implant. Data were collected in various body positions (supine, sitting, lying, right and left decubitus) and a 24 h dynamic ECG monitoring (Holter) was performed at the 3rd month follow-up in 172 patients.

Follow-up data discriminate results for sex, body mass index (BMI), for PM implant side and for atrial position of the dipole (exit of superior vena cava [SVC], high atrium [HA], mid atrium [MA] and low atrium [LA]).

**Results**

CAC is defined as a pacing giving 95-100% of constant and consecutive atrial capture during the entire period of observation. CAC was assessed programming a PM pacing rate 10 bpm higher than the intrinsic rate of the patient and a pulse amplitude 0.5 V over the OLBI atrial pacing threshold. Data are reported in Table 1 and are expressed as percentage of patients showing CAC at each body position during follow-up. At the 3 months follow-up the CAC (@ ATP at supine) was also assessed in relation to the position of atrial dipole giving the following results: SVC 100%, HA 77.7%, MA 82.1% and LA 50.0%.

90 days after implant, a 24 h Holter monitoring was performed in 135 patients (all with EIKOS SLD). The PM was programmed in DDD mode, basic rate at 15-20% over the patient sinus rate at rest and OLBI pulse amplitude 1.5 times the threshold value. 118/135 patients (87.4%) showed CAC during the entire 24 h period. In remaining 17/135 patients (12.6%), intermittent losses of atrial capture were associated to orthostatic position (6/17 patients) or at night (11/17 patients). Any symptoms related to losses of atrial capture or PNS was reported by these patients.

The data collected in CAC allow some notes concerning the first side effect of single lead DDD pacing: the inconstant atrial capture.

| discriminated group | n. pts | dis. | day 30 | day 90 | day 180 | day 360 |
|---|---|---|---|---|---|---|
| whole | 250 | 15.2 | 16.5 | 13.1 | 15.6 | 14.4 |
| males * | 150 | 10.0 | 12.9 | 4.8 | 8.6 | 6.7 |
| females * | 100 | 24.0 | 21.8 | 24.2 | 26.0 | 26.3 |
| left implants ** | 132 | 18.1 | 16.5 | 14.7 | 14.9 | 17.0 |
| right implants ** | 118 | 12.7 | 16.5 | 11.6 | 16.1 | 12.5 |
| dipole position SVC | 8 | n.a. | n.a. | 0 | n.a. | 0 |
| dipole position HA | 95 | n.a. | n.a. | 13.8 | n.a. | 12.2 |
| dipole position MA | 112 | n.a. | n.a. | 14.2 | n.a. | 18.1 |
| dipole position LA | 35 | n.a. | n.a. | 8.3 | n.a. | 0 |

*Table 2. Ocurrence of phrenic nerve stimulation at supine (PNS). Total number (N. pts) of all patients and percentages of patients showing PNS are given for different discriminated groups (sex, implant position, dipole position) at discarge (dis.) and follow up 1, 3, 6, 9, and 12 months after implant. Statistical difference between male and female group* is significant ($p<0.01$) ,whereas, statistical difference between left and right implants ** is not.*

a) The free floating status of the atrial dipole is the first and major responsible of intermittent lack of atrial capture. This condition is still present at one year from implant.
b) CAC is higher when the dipole is positioned at the exit of SVC since in this position the lead travels closer to active myocardium, but when patient changes its posture from supine to orthostatic or to lateral decubitus the dipole may respectively rise inside SVC, far from excitable tissues, or move away the atrial wall loosing CAC.
c) OLBI stimulation significantly improves atrial capture, but CAC is not achieved in the 100% of patients.

The occurrence of PNS, expressed as the percentage of patients showing evident stimulation of phrenic nerve at supine and with OLBI pulse amplitudes < 4.8 V and 0.5 ms pulse duration, are shown in Table 2.

Looking at occurrence of PNS in the whole group of patients a first comment can be made: with OLBI pacing technique combined to a straight single AV lead, PNS can not be completely avoided, as it depends onthe free floating condition of the atrial dipole that moves randomly inside the right atrium.

When data analysis is performed in discriminated groups, an astounding difference in PNS occurrence between male and female patients is statistically manifest. Since anatomy and physiology do not suggest any justification to such phenomenon, PNS data were subsequently related to the BMI (body weight / height$^2$) of the patient, which differs between sexes for well known anatomical reasons. The results of this analysis for patients showing PNS and patients without PNS are depicted in Figure 1. In the figure, two separate gaussian distribution are evident. All patients showing PNS had a low BMI, which upper limit was 25 for male and 23 for female patients. Over the above BMI limits PNS never occurred. Then BMI seems to be in direct correlation with the distance between the position of the dipole inside the right atrium and the anatomic area in which the phrenic nerve is traveling. Since the electric field created by OLBI stimulation is mostly concentrated in the vicinity of the dipole and it protrudes only in the direction of the field vector toward the PM case, a little variation in thickness of the layer of tissues between atrial myocardium and mediastinum (i.e. a BMI variation) may determine the occurrence or not of PNS.

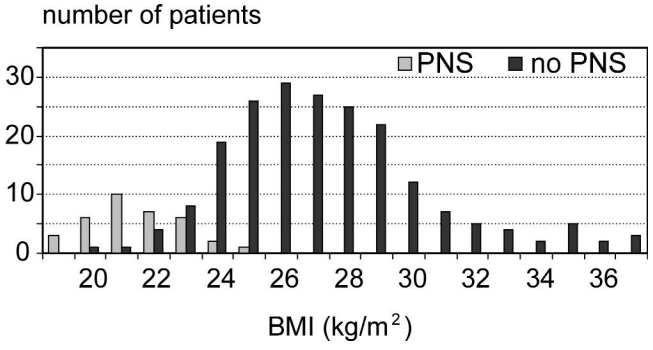


*Figure 1. BMI distribution for patients with and without phrenic nerve stimulation (PNS). PNS was detected below up to an upper limit of 25.*

## Discussion

Some additional comments on PNS occurrence concern its correlation to the PM implant site and dipole position.

Leads implanted by left access constantly show a slightly higher PNS occurrence than those implanted in the right side. A possible reason is that leads inserted by left access travel close the atrial wall facing mediastinum. This condition improves atrial pacing threshold but may also increase the probability to induce PNS. The statistical difference between the two groups is not significant but, nevertheless, there is an evident trend during the entire follow-up.

About dipole position PNS data concerning HA and MA has to be taken in consideration only, because the very small number of patients in which the dipole was positioned in SVC or in LA. LA group was bigger at discharge (35 patients) but at the 3rd month follow-up only 5 dipoles were found in their original position, all other rised in MA. PNS occurrence is slightly higher in HA than in MA but the difference is not statistically significant.

This second group of data and comments allow the following notes on the second side effect of single lead DDD pacing: the occurrence of phrenic nerve stimulation.

a) Floating nature of atrial dipole also influences PNS.
b) Distance between atrial myocardium and the traveling site of the phrenic nerve is responsible of PNS occurrence. At present time BMI seems to be the sole parameter allowing a reliable selection of patients who may not show this adverse effect.
c) PM implant site and atrial dipole position play a minor role in PNS. The distance between dipole and phrenic nerve is closer when lead is inserted by left access.

The third side effect of single lead DDD pacing: the thoracic muscles contraction was never reported during whole follow-up. Thus, this complication seems to be totally avoided with OLBI stimulation, since in this approach the flows of electric current traveling from and to the PM case are negligible.

## Conclusions

During 90 s several groups of investigators attempted to demonstrate that DDD pacing was feasible using unipolar stimulation through one of the floating atrial electrodes of a single AV lead. Major side effects as inconstant atrial capture, phrenic nerve stimulation and thoracic muscles contraction were reported in more than 50% of the patients initially submitted to this pacing approach and this percentage increased during implant maturation.

Recent introduction of OLBI technique consistently reduces the occurrence of side effects allowing a constant, stable and painless single lead DDD stimulation in more than 80% of patients implanted with this new pacing system. The results of this extensive investigation show that OLBI atrial stimulation can be considered as a reliable alternative to the conventional dual lead approach for back-up atrial pacing in carefully selected patients with advanced AV block and sporadic or mild chronotropic incompetence.

However, to reach a true "side effect-free" primary atrio-ventricular pacing with a single AV lead, some additional improvements should be made. Most of them has to be addressed in changing the lead design, pre-shaping its atrial portion in order to achieve a more stable positioning of the atrial dipole close to the myocardium and far from the phrenic nerve. Electrode geometry as to be improved as well, since floating ring electrodes waste most of the energy in the neighboring blood.

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