A small clinical-ECG/VCG detail is the diagnostic clue… Did you get it?

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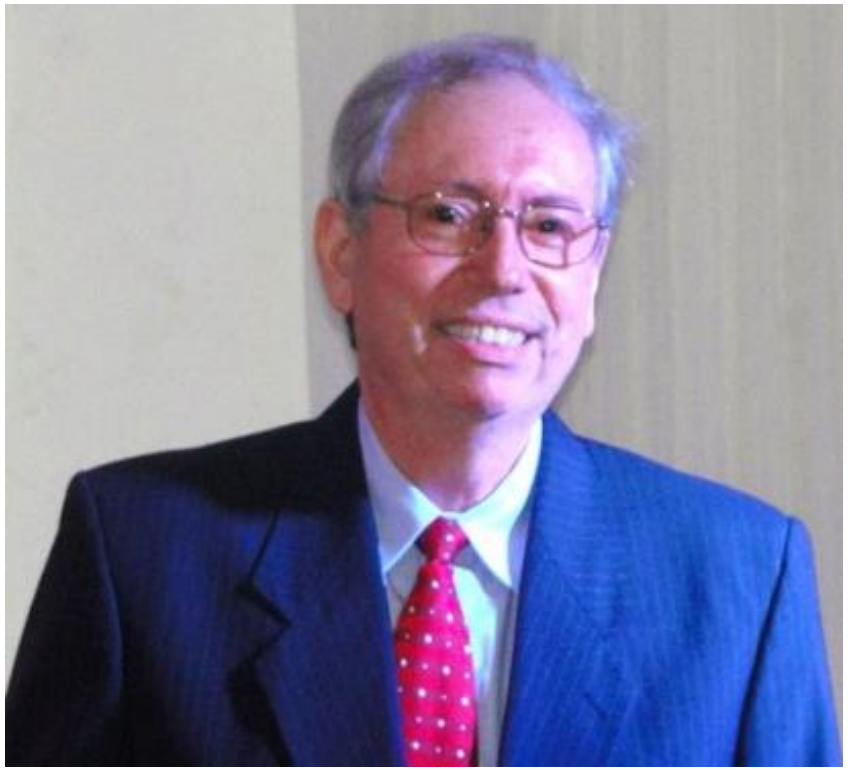

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Portuguese: Apresentação do caso

Paciente masculino, branco, 73 anos, advogado, encaminhado por neurologista, com quem estava sendo estudado devido a déficit cognitivo, para avaliação cardiológica. Refere ser hipertenso de longa data e concomitantemente ser portador de cardiomiopatia hipertrófica familiar (familiares de primeiro grau – 2 irmãos - são portadores tanto de hipertensão quanto de cardiomiopatia hipertrófica). Refere também três episódios de palpitações rápidas e irregulares, revertidas espontaneamente, tendo sido registrada a última, onde se demonstra fibrilação atrial.
Em uso regular do betabloqueador atenolol 50 mg/dia + olmesartana medoxomila 40 mg/dia + clortalidona 12,5 mg/dia + espironolactona 25 mg/dia + rusovastatina 5 mg/dia.
Realizamos ECG e VCG, assim como ecocardiograma e ressonância nuclear magnética do coração. Os dois últimos exames confirmaram a cardiomiopatia hipertrófica subaórtica (espessura septal alta de 24 mm) e de parede livre 14 mm. Importante obstrução na via de saída do ventrículo esquerdo, e característico movimento anterior sistólico do folheto anterior da válvula mitral. Moderado aumento do átrio esquerdo, e refluxo mitral leve a moderado.
Exame físico: lúcido, corado, pressão arterial 170/95 mmHg, pulsos regulares e lentos (FC 52 bpm), ausência de congestão venosa no pescoço, ictus cordis localizado no sexto espaço intercostal esquerdo, a 1,5 cm por fora da linha hemiclavicular, intenso, e aproximadamente com 2 cm de diâmetro. Na ausculta, quarta bulha pré-sistólica e sopro sistólico regurgitante ++/4 foco mitral. Pulmões: limpos, murmúrio vesicular presente e sem ruídos adventícios. O restante nada digno de nota.
Perguntas:

1. Qual o diagnóstico eletrocardiográfico do ECG-1?
2. Qual o diagnóstico do ECG-2?
3. Qual o diagnóstico clínico?

English: Case presentation

73-year-old male, Caucasian, lawyer, referred by a neurologist, with whom he was being studied due to cognitive deficit, for cardiac evaluation. He refers to be a long-standing hypertension and concomitantly carrier of familial hypertrophic cardiomyopathy (first-degree relatives - 2 siblings - are carriers of both hypertension and hypertrophic cardiomyopathy). He also refers three episodes of rapid and irregular palpitations, reversed spontaneously, and the last one was recorded, where atrial fibrillation is shown.

He is in regular use of the beta-blocker atenolol 50 mg/day + olmesartan medoxomil 40 mg/day + chlortalidone 12.5 mg/day + spironolactone 25 mg/day + rusovastatin 5 mg/day.

We performed ECG and VCG, as well as echocardiogram and nuclear magnetic resonance of the heart. The last two exams confirmed subaortic hypertrophic cardiomyopathy (high septal thickness 24 mm) and free wall 14 mm. Significant obstruction in the left ventricular outflow tract, and characteristic systolic anterior movement of the mitral valve anterior leaflet. Moderate enlargement of the left atrium, and mild to moderate mitral reflux.

Physical examination: lucid, stained, blood pressure 170/95 mmHg, regular and slow pulses (HR 52 bpm), absence of venous congestion in the neck, ictus cordis located in the 6^{th} left intercostal space, at 1.5 cm outside the hemiclavicular line, intense, and approximately 2 cm in diameter. In the auscultation, 4^{th} pre-systolic sound and regurgitant systolic murmur ++/4 mitral focus, irradiated to axilla. Lungs: clean, Presence of vesicular murmur, without adventitious noises. The rest is not relevant to be noted.

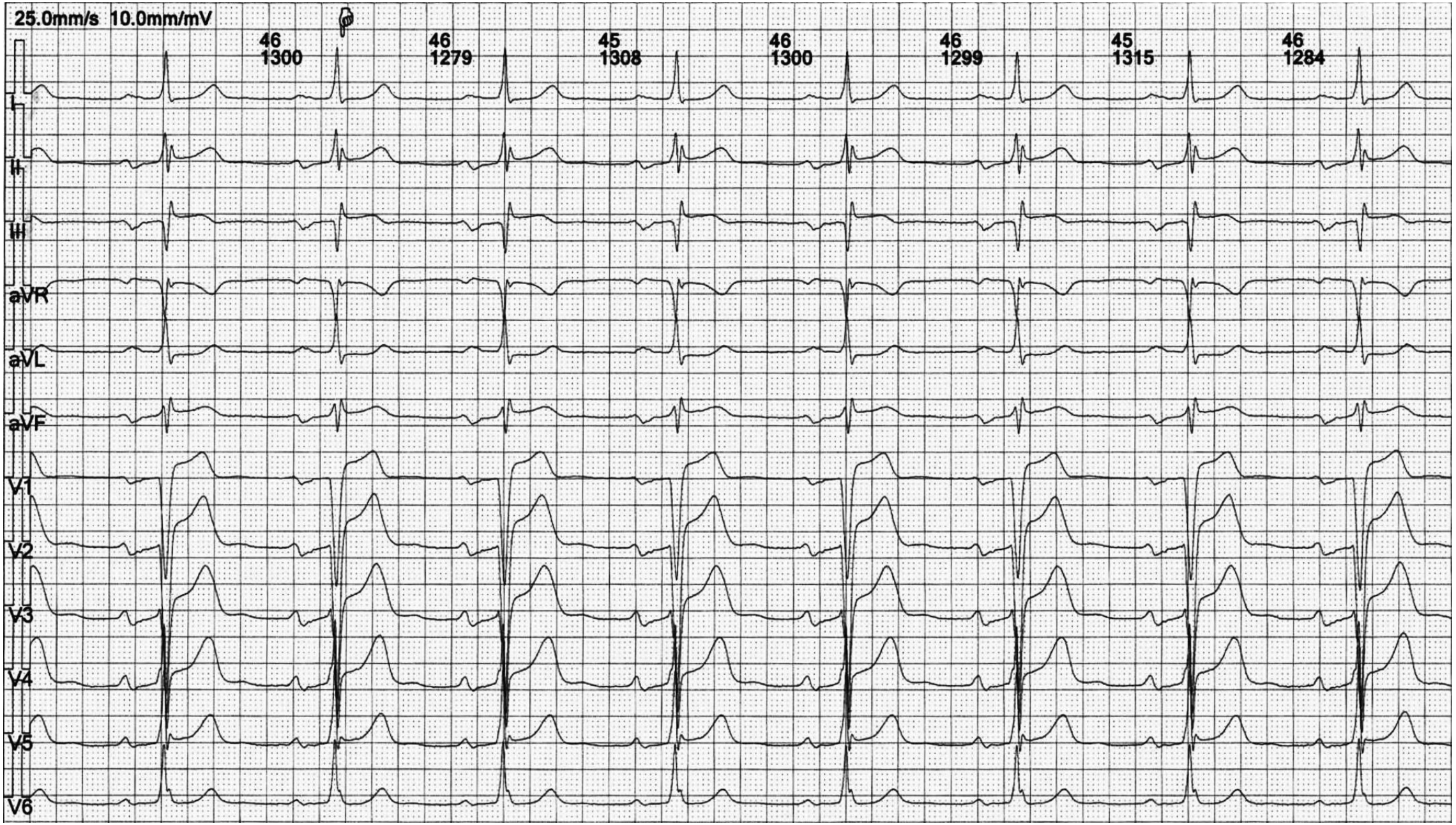
Questions:

Which is the ECG diagnosis of ECG-1?

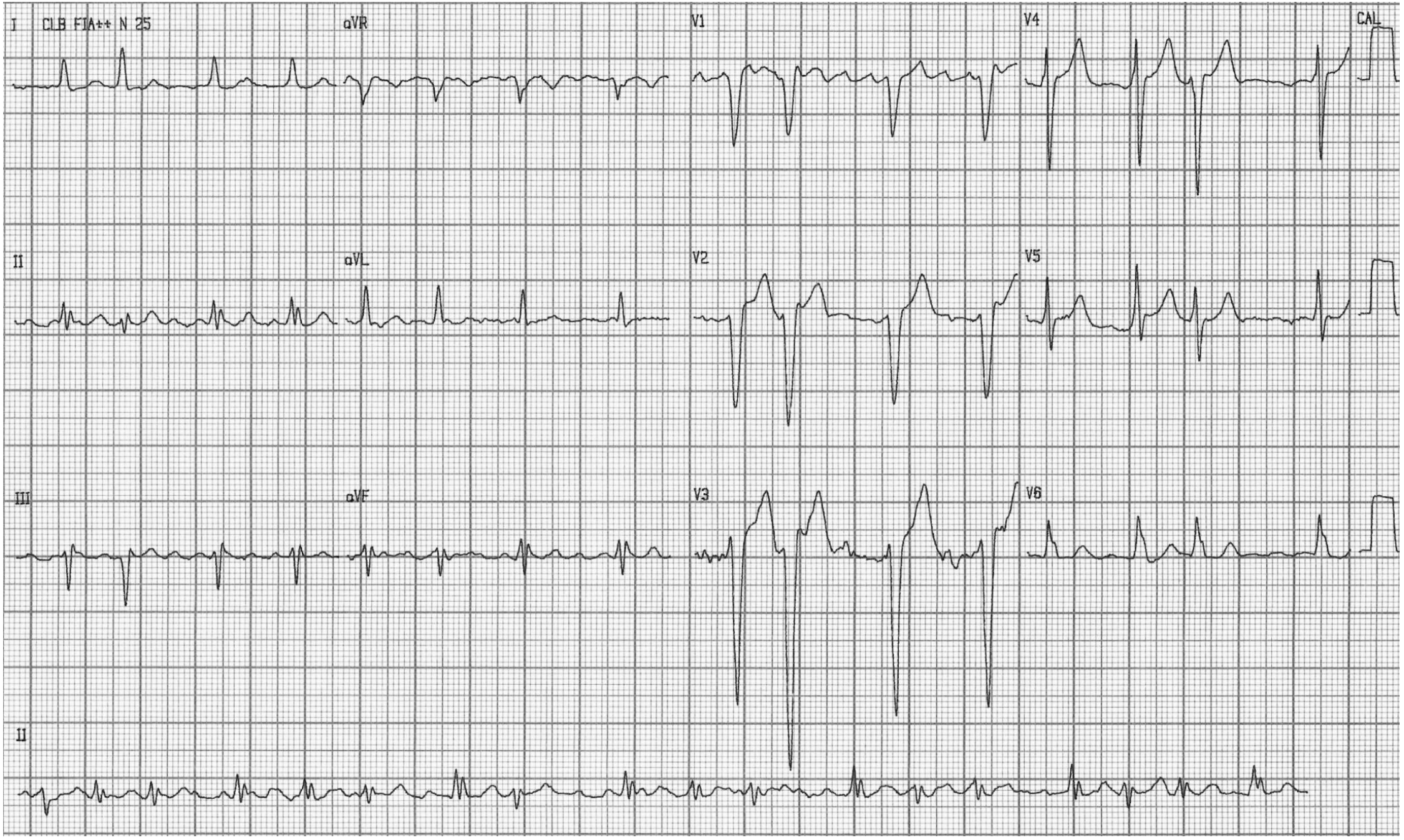
Which is the ECG diagnosis of ECG-2?

Which is the clinical diagnosis?

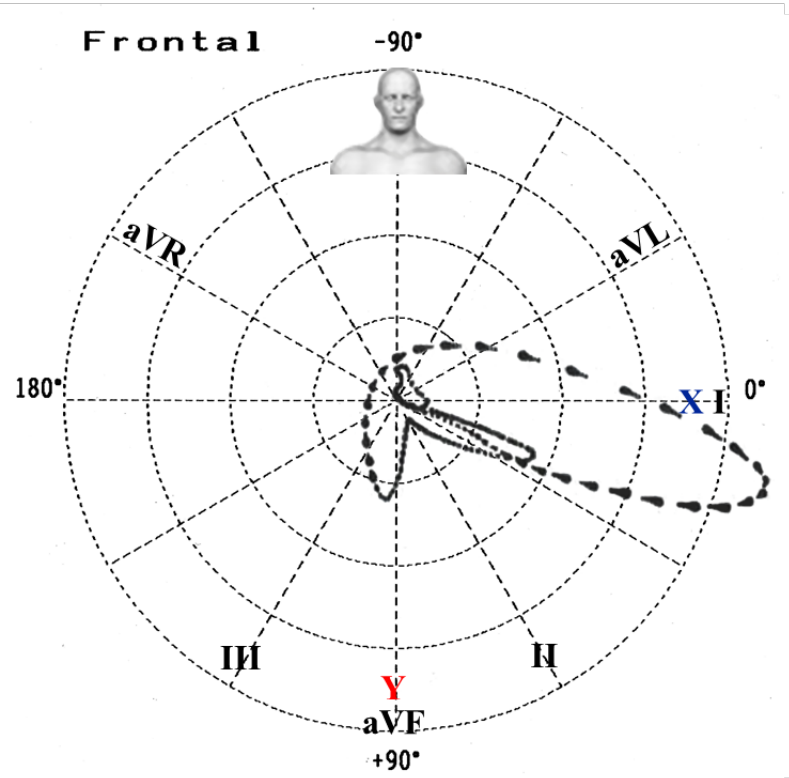
ECG-1 at admission

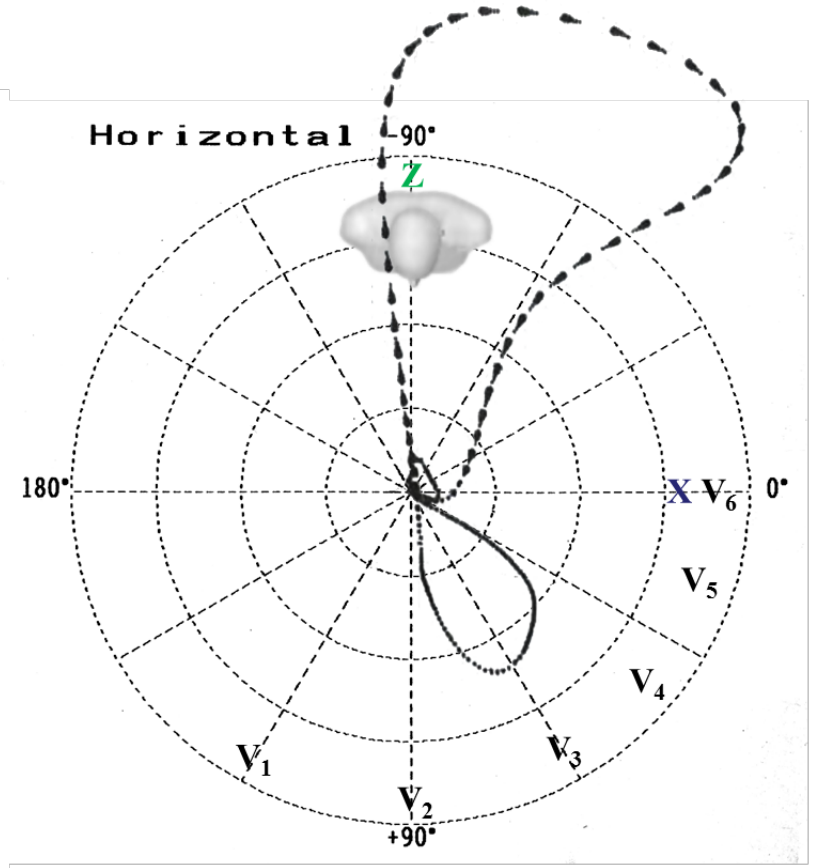


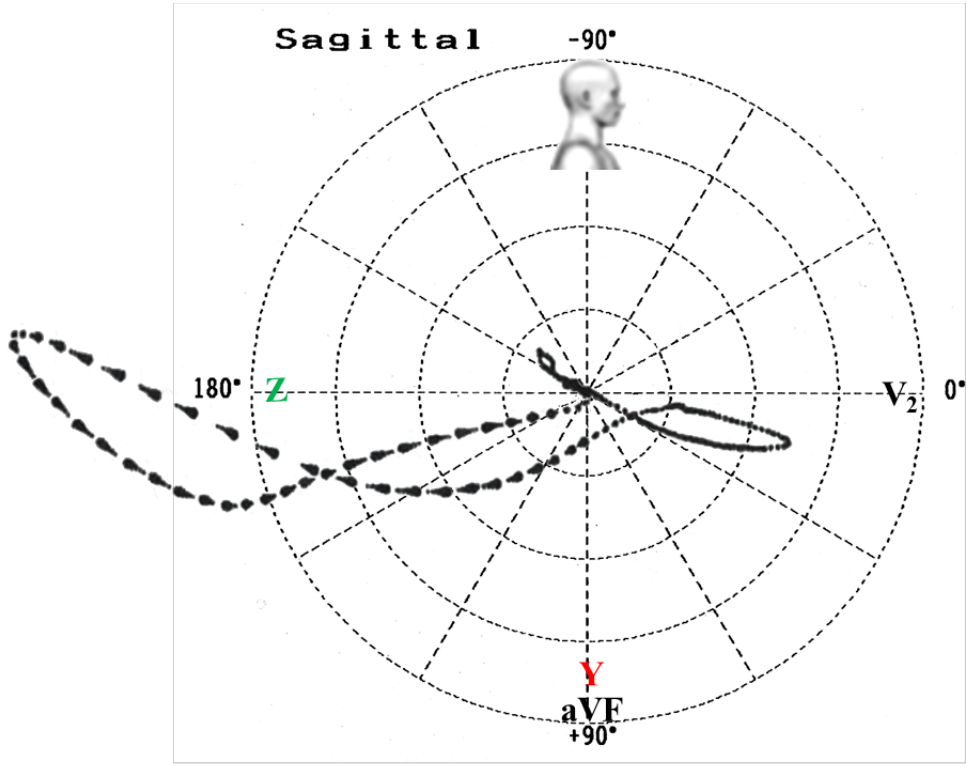
ECG-2 during rapid and irregular palpitations with spontaneous reversion (2015)



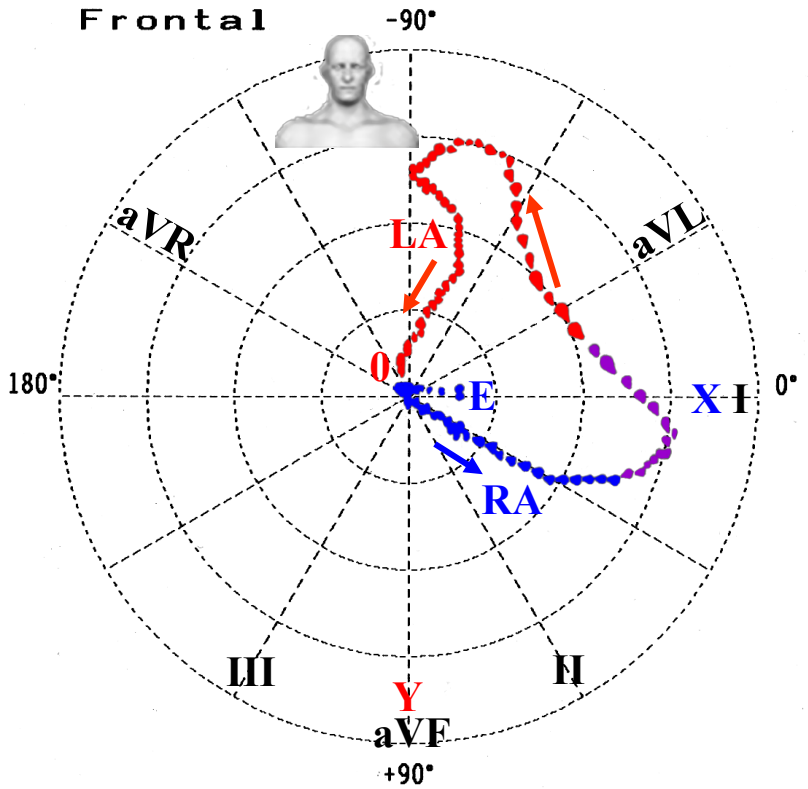
VCG in the three planes

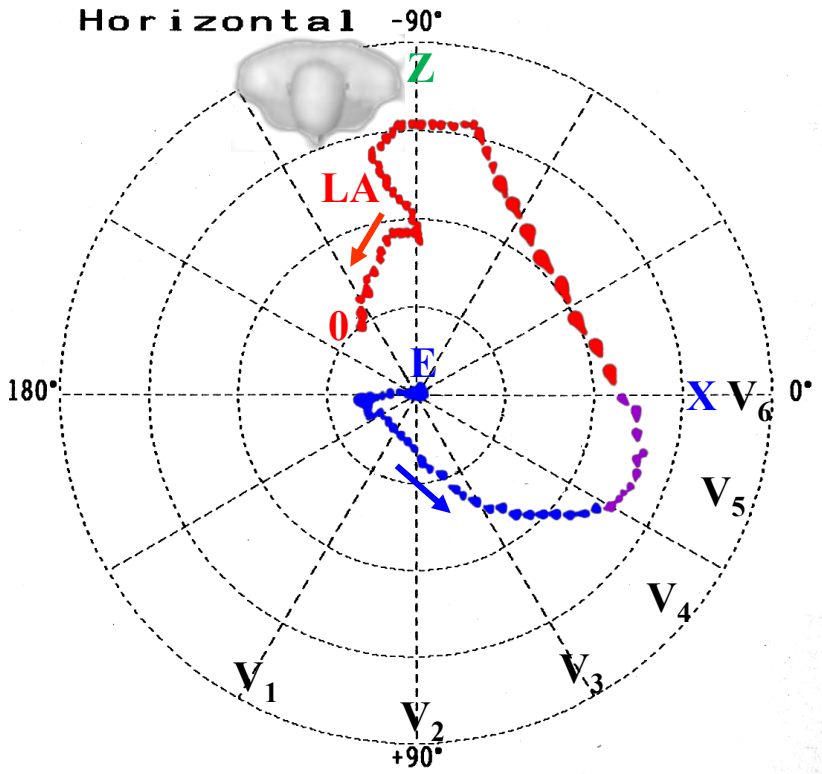


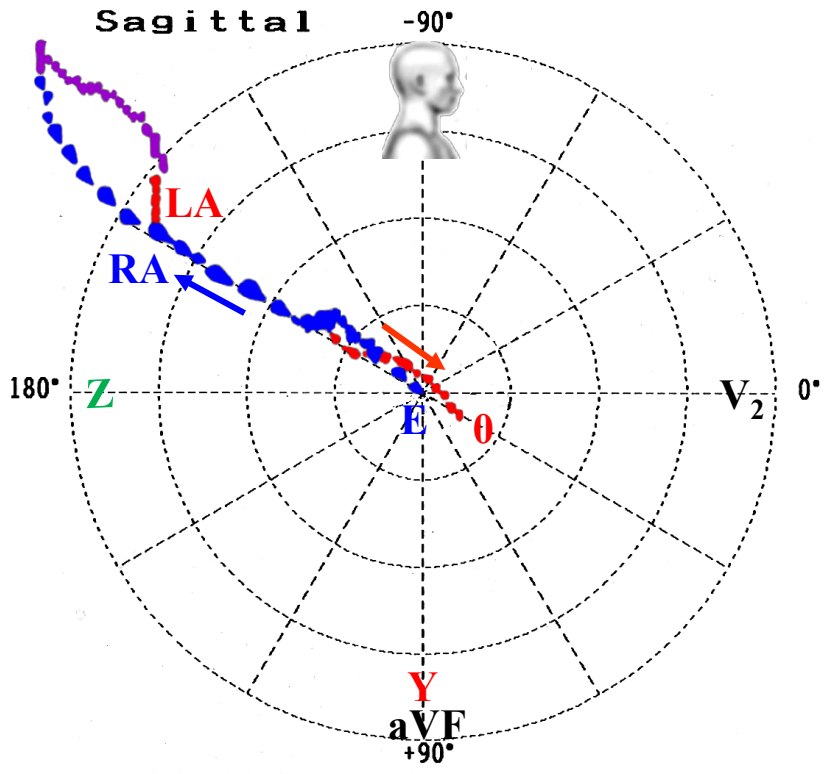




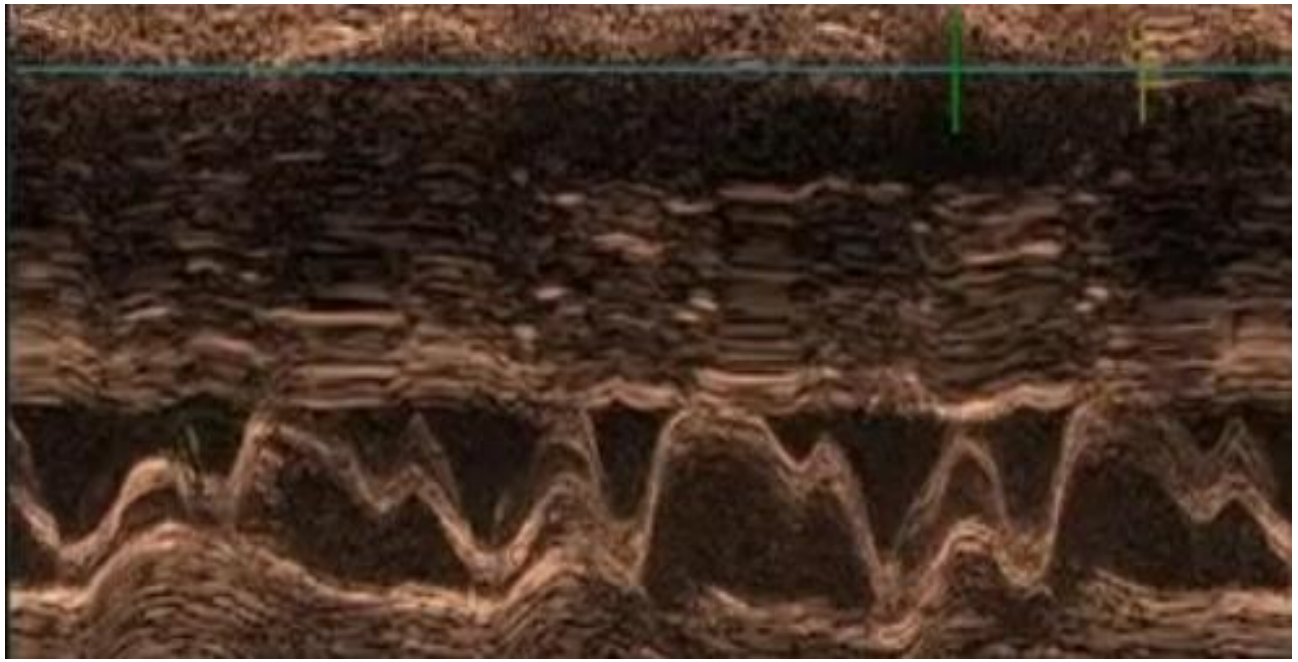
Magnified P-loop (32x) in the three planes

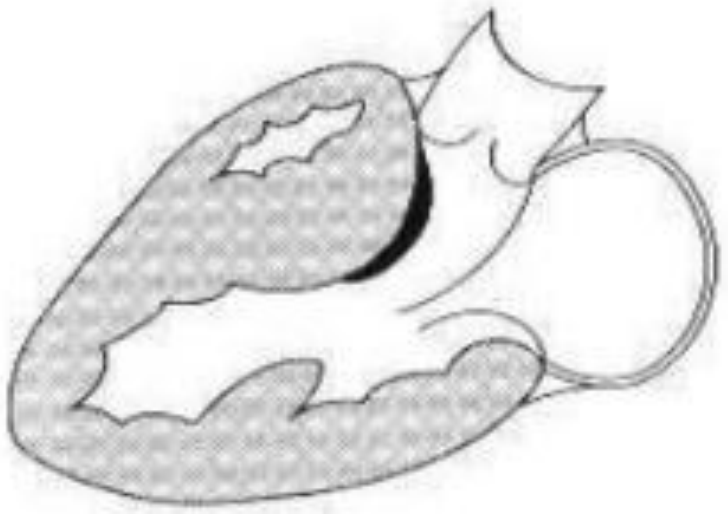






Echocardiogram M-mode





Colleagues opinions

The ECG looks like LVH (Cornell criteria#) and Left atrial abnormality. Will learn VCG abnormalities from the masters.

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Cornell index (CI), Casale criteria or Cornel criteria: CI = RaVL + S V3 > than 28 mm in men or > 20 mm in women indicates LVH.
Cornell product (Molloy 1992) 1985; (CorP.)*Cornell voltage-duration product It is the product of QRS voltage and QRS duration (QRS voltage-duration product); Cornell voltage-duration product (RaVL + SV3 with 6 mm added in women x QRS duration). Values ≥2440 mm/ms are diagnostic of LVH (Positive criteria of LVH CP≥2440 mm x ms).
The Cornell product is a useful ECG marker, reflecting not only left ventricular mass but also LV geometry and diastolic function in Japanese hypertensive patients (**Shira 2007).**
Reduction in Cor P ECG LVH during antihypertensive therapy is associated with fewer hospitalizations for HF, independent of blood pressure lowering, treatment method, and other risk factors for HF. (**Okin 2007**).

Spanish

El ECG #1: ritmo sinusal 46 lpm, bloqueo AV 1° grado, bloqueo interauricular avanzado, sobrecarga auricular izquierda (criterio de Morris positivo en V1). Sobrecarga VI e hipertrofia VI. (Criterios de voltaje: índice de Sokolov-Lyon y de Cornell positivos), deflexión intrinsecoide > 50 mseg en V5 y V6). También se observa onda Q importante en DIII < 40 mseg y de mayor voltaje que onda R y onda T positiva (pseudoinfarto) en espejo de aVL. también fQRS en cara inferior (predictor de eventos arritmicos potencialmente fatales). Presencia en QS desde V1-V2 con SupraST > 0.1 mV hasta V4 y onda T positiva Es visible también pseudo onda delta en V4. Probable onda J en V5 y V6.
Signos electrocardiográficos de miocardiopatía hipertrófica obstructiva.
ECG #2: Fibrilación auricular de alta respuesta ventricular.
Diagnóstico clínico : Síndrome de Bayés. Miocardiopatía hipertrófica obstructiva, insuficiencia mitral.
Los saludo afetuosamente

Dr Juan Carlos **Manzzardo**
Mendoza Argentina

English

ECG # 1: sinus rhythm, heart ratei 46 bpm, 1st degree AV block, advanced interatrial block, left atrial enlargement (positive V1 Morris criterion). LAE+ LVH (Voltage criteria: positive Sokolov-Lyon and Cornell index), intrinsecoide deflection> 50 ms in V5 and V6). We also observed a significant Q wave in III <40 msec and higher voltage than R wave and positive T wave (pseudoinfarction) in aVL mirror. Also fQRS on the lower face (predictor of potentially fatal arrhythmic events). Presence in QS from V1-V2 with SupraST> 0.1 mV to V4 and positive T wave It is also visible pseudo delta wave in V4. Probable J wave in V5 and V6.
Electrocardiographic signs of obstructive hypertrophic cardiomyopathy.

ECG # 2: Atrial fibrillation with high ventricular response.

Clinical diagnosis: Bayés syndrome. Obstructive hypertrophic cardiomyopathy, mitral insufficiency.
Affectionately

Juan Carlos Manzzardo MD
Mendoza Argentina

Queridos Andrés y Raimundo,

Por fin llegó un VCG de bloqueo Avanzado interauricular (BIA-A)….Bellísimo. Ya os he comentado que creo que la VCG puede facilitar el diagnóstico y sugerir grado y localización de la fibrosis…..Para ello se necesita un gold estándar de fibrosis que es la resonancia magnética. Creo podría servir como surrogate la "speckle-tracking" ecocardiografica.

Raimundo y yo ya hablamos de esto en Roma….Ánimos!!

Un abrazo,

Antonio

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English

Dear Andrés and Raimundo

At last came an Advanced Interatrial Block VCG (A-IAB) ... .BEAUTIFULL!!!!!. I have already commented that I believe that the VCG can facilitate the diagnosis and suggest the degree and location of fibrosis ... .. For this you need a Gold standard fibrosis which is the MRI. I think it could serve as surrogate speckle-tracking echocardiography.

Raimundo and I already talked about this in Rome .... Few days ago

A hug,

Spanish

Hola: Hermosa presentación
En contexto de apreciaciones referidas por Dr Nikus y Antoni el VCG muestra:

1. Con un bucle de P en el plano frontal orientado en cuadrante superior izquierdo y eje máximo de P en - 40° por influencia de la despolarización de AI que se realiza de abajo hacia arriba (y no a la inversa)por bloqueo de las vías o fibras ("autopistas" al decir de Bayes) de Bachman configurando un bloqueo inter auricular avanzado.
2. El bucle del QRS en el plano horizontal totalmente hacia atrás es sugestivo de fibrosis de segmentos anteroseptal que se correlaciona con el QRS. Además, muestra características de agrandamiento de VI.

Saludos cordiales
Jan José Sirena Santiago del Estero Argentina

English

Hi, beautiful presentation!
In the context of the assessments referred to by Dr Nikus and Antoni the VCG shows:
The P-loop axis in the frontal plane is oriented in the upper left quadrant (P- maximum axis in - 40 °) by influence of the depolarization of LA that is performed from bottom to top (and not vice versa) by blocking the tracks or fibers ("freeways" as Bayes says) by setting up an advanced inter-atrial block.(A-IAB)
The QRS loop in the PH is directed fully backward and leftward. It is suggestive of anteroseptal segment fibrosis correlates with the QRS pattern. In addition, it shows features of LVH.
Best Regards
Juan José Sirena Santiago del Estero Argentina

Hello!

1. Prolonged PQ interval. Interatrial block (?). LVH with mild LV strain.

2. Atrial flutter, ventricular extrasystole

3. HCM. Bayés syndrome.

Best regards

Kjell Nikus

Tampere

Finland

Final conclusions by

P –wave duration ≥ 120ms + biphasic - positive-negative-"plus-minus" P wave in inferior leads II, III and aVF + caudo-cranial left atrial activation + repetitive paroxysmal atrial fibrillation episodes: **Bayes' syndrome. Advanced, "third-degree" or "complete" interatrial block (A-IAB) associated with atrial Tachyarrhythmias = Bayés´s syndrome.**

+

Left Atrial Enlargement (LAE) (It is present in 90% of cases of advanced interatrial block (A-IAB). Bayés de Luna, et al perform the first consensus to separates A-IAB from **LAE** (**Bayés de Luna 2012**). The longer P-wave duration observed in HCM patients may be explained by a higher prevalence of block in one or more of the interatrial conduction routes. (**Holmqvist 2007**)

+

LVH with strain pattern of repolarization, Cabrera LVH systolic type or VCG LVH type 1A (see in the next slides)

+

Familial Obstructive Hypertrophic Cardiomyopathy (HOCM)

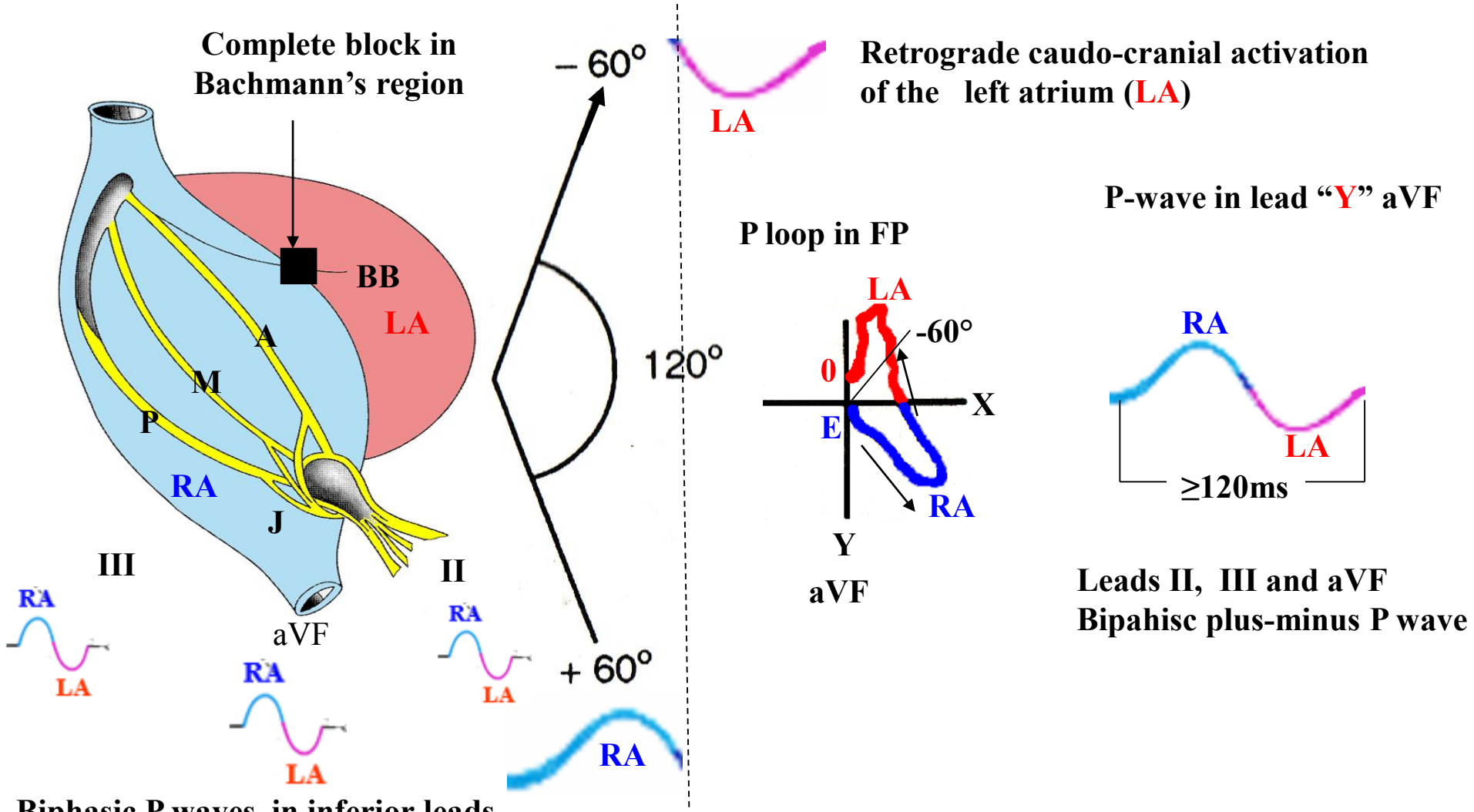
+

Systemic Hypertension

Interatrial block and Bayés syndrome overview

Interatrial block (IAB) is a ECG disturbance that entails a delayed conduction between the both atria during atrial depolarization. IAB has further been classified into partial IAB (pIAB) or second degree IAB, which is seen on the ECG as P-wave duration ≥ 120 ms, or advanced IAB (A-IAB) in which P wave duration ≥ 120ms with a biphasic positive-negative "plus-minus" P-wave in the inferior leads (II, III, and aVF). In addition the P-loop of the VCG show a characteristic P-loop pattern in the FP: the orthogonal lead "**Y**" lead (+90°/-90°) plus-minus with the final negative portion ≥40 ms, consequence of retrograde caudo-cranial activation of the left atrium (**LA**) with final portion of P-loop delayed, notches and slurring in the last portion. (**Bayes de Luna 2012**) This pattern arises owing to a delay of conduction at the Bachmann region (old Bachman bundle) resulting in retrograde, caudocranial conduction to the left atrium (**LA**) through the coronary sinus musculature (**Cosio 2004**). However, if the wave passes through the rim of the fossa ovalis, then retrograde activation may not necessarily occur.(**Tse 2017**) This abnormal caudal-cranial activation of the *LA* owing to fibrosis of the Bachmann region predisposing patients to interatrial dyssynchrony. The presence of Bayés syndrome in patients with atrial pacing has not been sufficiently explored. Clinicians must be cognizant of this possibility as the early identification of this pattern suggests the need for closer monitoring of AF and prophylaxis of cardioembolic events.(**Britton 2017**). Dr Bayés de Luna was the first who provided a clear description of atrial conduction block in 1979, classifying them into either inter- and intra-atrial (**Bayés de Luna 1979**). In recognition of his numerous contributions to the understanding of IAB (**Bayes de Luna 1985**), this syndrome was named Bayés syndrome by Conde and Baranchuk, (**Conde 2014**). The clinical relevance of Bayés syndrome lies in the fact that is a clear arrhythmological syndrome and has a strong association with supraventricular arrhythmias, particularly atypical atrial flutter and AF and it is independently associated with an increased risk for non-lacunar cardioembolic stroke. Likewise, can be the cause of some cryptogenic strokes, and be related to clinically silent cerebral ischemia and vascular cognitive impairment(such as the present case), or even, vascular dementia (**Arboix 2017**). Likely owing to delayed, heterogeneous activation of the **LA** (**Bayés de Luna 2012**). We described and old man wit systemic hypertension and OH-HCM whose ECG/VCG shows typical A-IAB, LVH associated with repetitive episodes of paroxysmal AF which characterizes the so-called Bayes syndrome an under-recognized clinical syndrome. Positive-negative biphasic or "plus-minus" P-wave + P-duration ≥ 120ms + AF episodes: Bayés syndrome owing to fibrosis of the Bachmann region predisposing patients to interatrial dyssynchrony and AF. Bayes' syndrome has been identified in numerous patient populations, but its presence in patients with atrial pacing has not been sufficiently explored. Clinicians must be cognizant of this possibility as the early identification of this pattern suggests the need for closer monitoring of AF and prophylaxis of cardioembolic events. IAB may be of 1st degree (P-wave duration >120 ms), **A-IAB**: P wave≥ 120ms biphasic [±] in inferior leads, and 2nd degree when these patterns appear transiently in the same ECG recording (atrial aberrancy). These P-wave patterns are due to a block because they may (a) appear transiently, (b) be without associated **LAE**, and (c) may be reproduced experimentally.

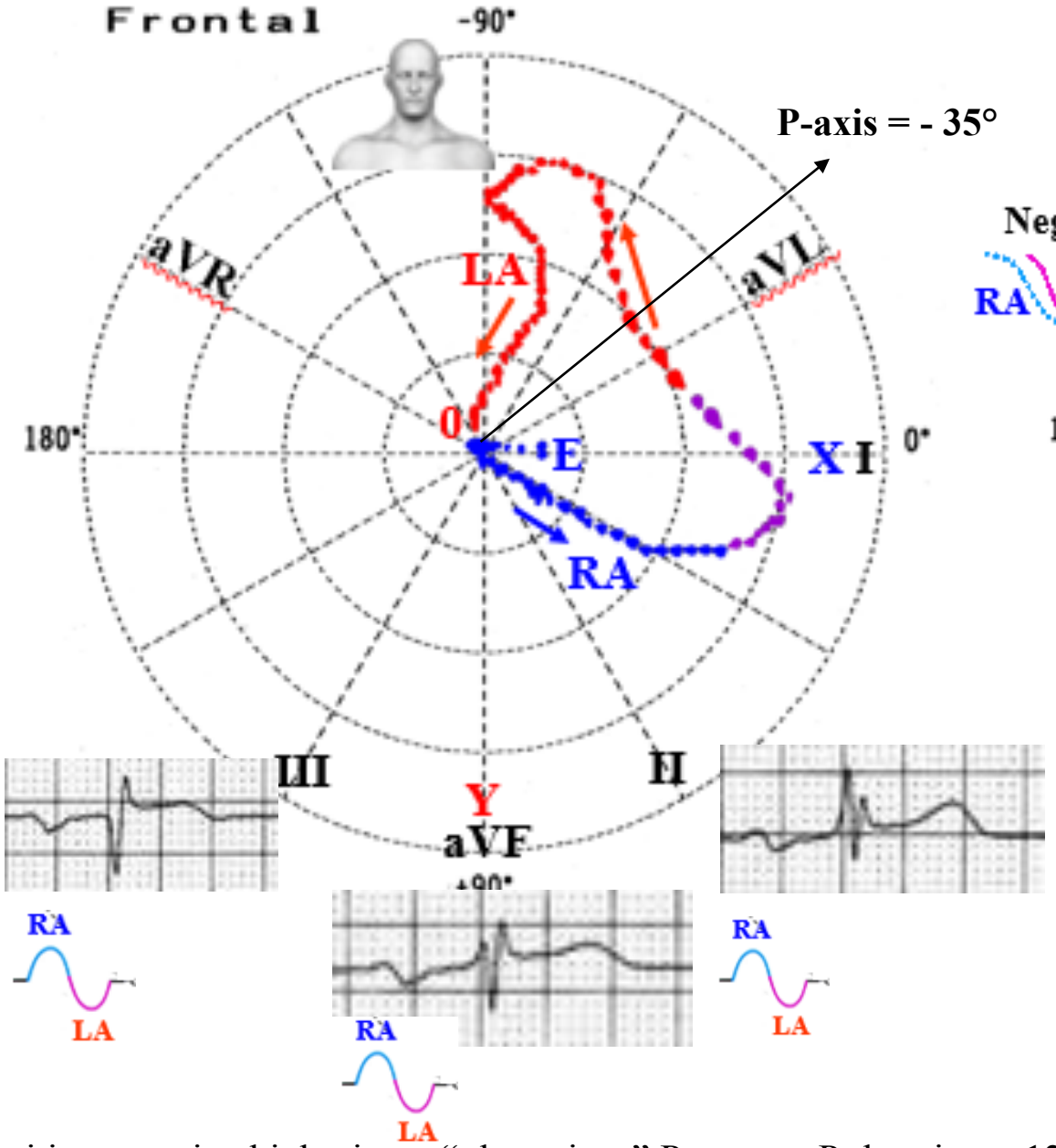
Third degree block, complete or advanced interatrial block: P-duration ≥120ms+ biphasic P-wave in inferior leads



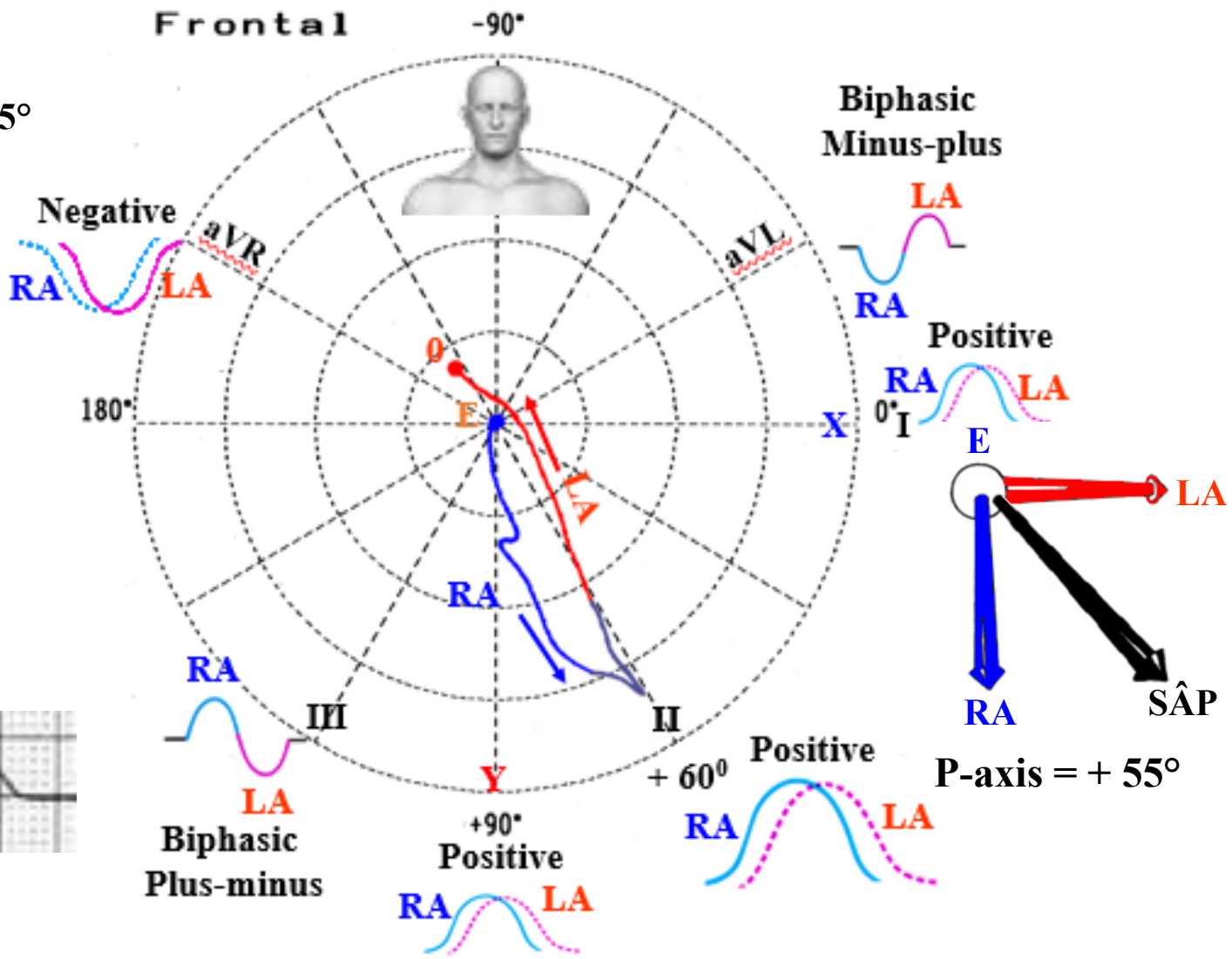
Third Degree, A-IAB or complete IAB

Electrical impulse is blocked/delayed in Bachmann's muscular interatrial bundle or region (BB), but retrograde left atrial activation usually occurs.(**Ariyarajah 2005**) Note the existence of an open angle between the vector of the first portion of P wave (**RA**) and the last portion (**LA**). Electrophysiological study demonstrates retrograde activation of the **LA**. Consequently P loop/wave in orthogonal lead "**Y**", aVF and III is biphasic plus-minus ±. LA activation occurs by an alternate route rather than proceeding from right to left via the BB.(**Spodick 2007**)

P-loop and inferior P-waves in the frontal Plane in the present case (High magnification of the P loop (0.1 mV = 3 cm)

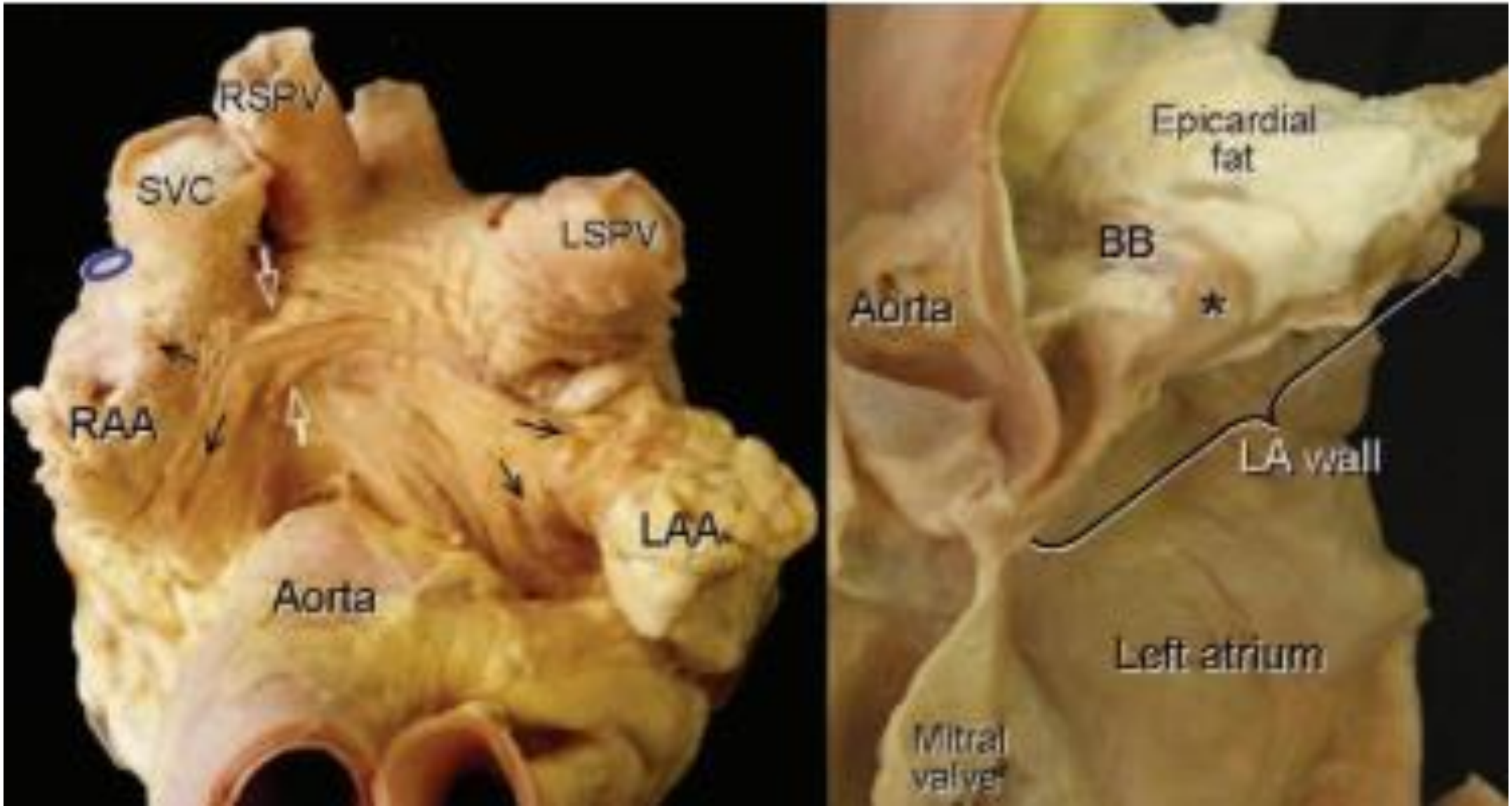


P-loop and P-wave polarity in the frontal Planein normal cases (High magnification of the P loop (0.1 mV = 3 cm)

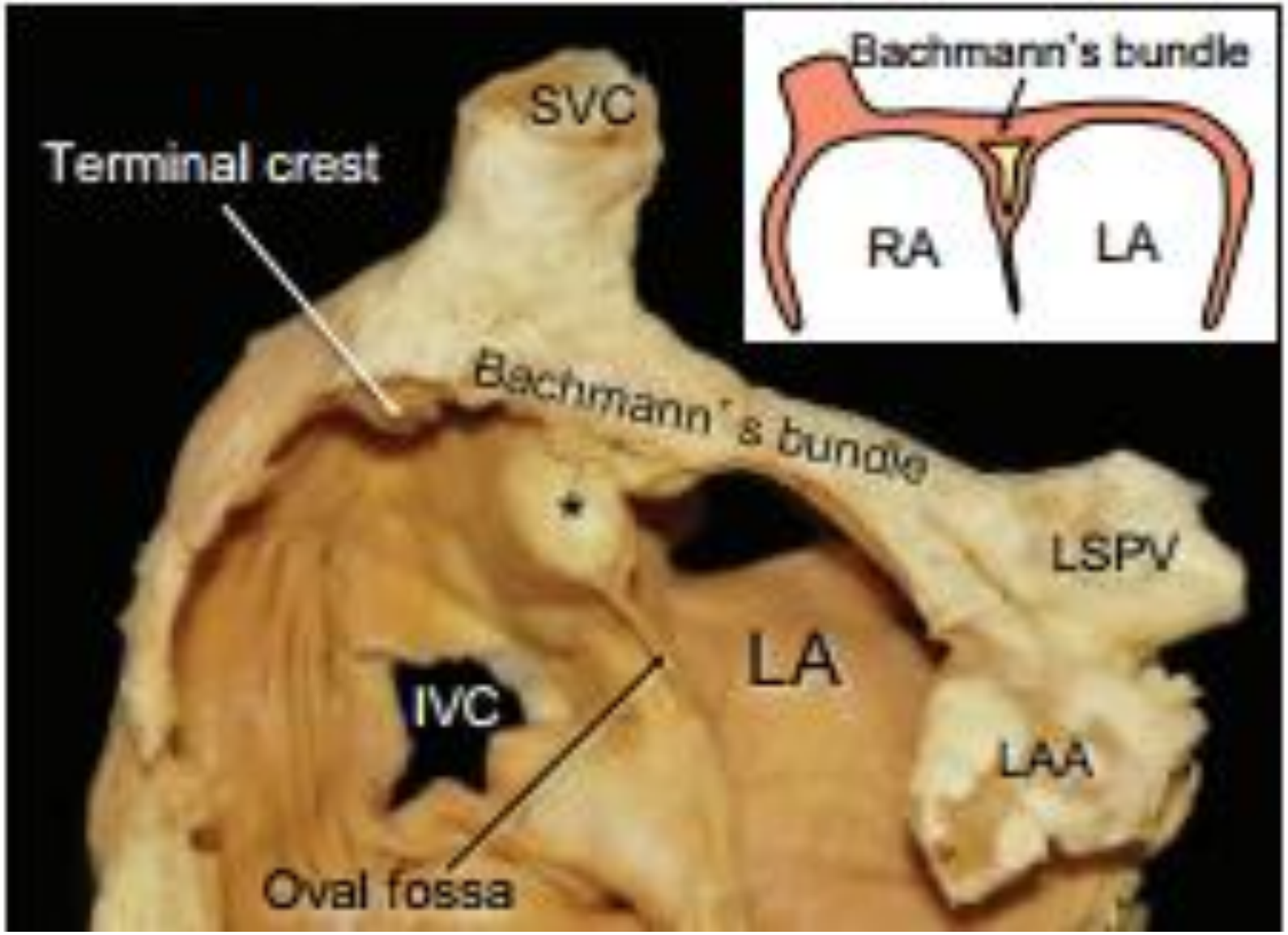


Positive-negative biphasic or “plus-minus” P-wave + P-duration ≥ 120ms (A-IAB) + repetitive AF episodes: Bayés syndrome

In 1963, Thomas N. James described 3 pathways connecting the sinus node to the atrioventricular node (AVN), namely the anterior, medial, and posterior internodal pathways (**James 1963**). Whether these conduction pathways were because of the presence of specialized conduction tissue or because of the anisotropic orientation of the muscle fibers remains controversial. Nevertheless, James described the anterior pathway as leaving the sinus node in anterior direction and giving off a secondary branch at the level of the superior vena cava to form BB.(**Bachmann 1916**) BB stretches subepicardially across the interatrial groove (septal raphe). It is at the interatrial groove that the BB can be identified as a discrete bundle (Figures next 2 slides) separated by fatty tissues from the infolded right atrial wall that is the limbus of the oval fossa. Notably, the bundle is not surrounded by a fibrous tissue sheath. Instead, the bundle is comprised of strands of atrial myocardium that are similarly aligned in parallel fashion. Its rightward and leftward extensions bifurcate to pass to either side of the right and left atrial appendages (**LAA**) (**Khaja 2003**). Although they can be traced to varying extents with blunt dissection, both extensions blend into the musculature of the atrial walls. The superior arm of the rightward extension arises in the region of the cavoatrial junction close to the site of the sinus node and in the vicinity of the sagittal bundle. The inferior arm arises in the subepicardium of the RA vestibule. Leftward, BB buttressing part of the anterior atrial wall with its thickness (figure next slide) is still traceable to where it encircles the neck of the **LAA** and blends in with the lateral atrial wall. The superior part traverses in the infolding of the atrial wall, known to arrhythmologists as the left lateral ridge, to pass in front of the orifices of the left pulmonary veins.(**Cabrera 2008**) The inferior part descends toward the atrial vestibule to combine with the circumferentially aligned myocardial strands in the subepicardium of the inferior wall. In contrast to the thinner distal extensions, BB's body across the interatrial groove is a broader band (see next 2 figures), with median measurements of 4 mm in thickness and 9 mm in height. It is described as trapezoidal shaped because of its short lower length (3 mm) and longer upper length (10 mm).(**Lemery 2003**)



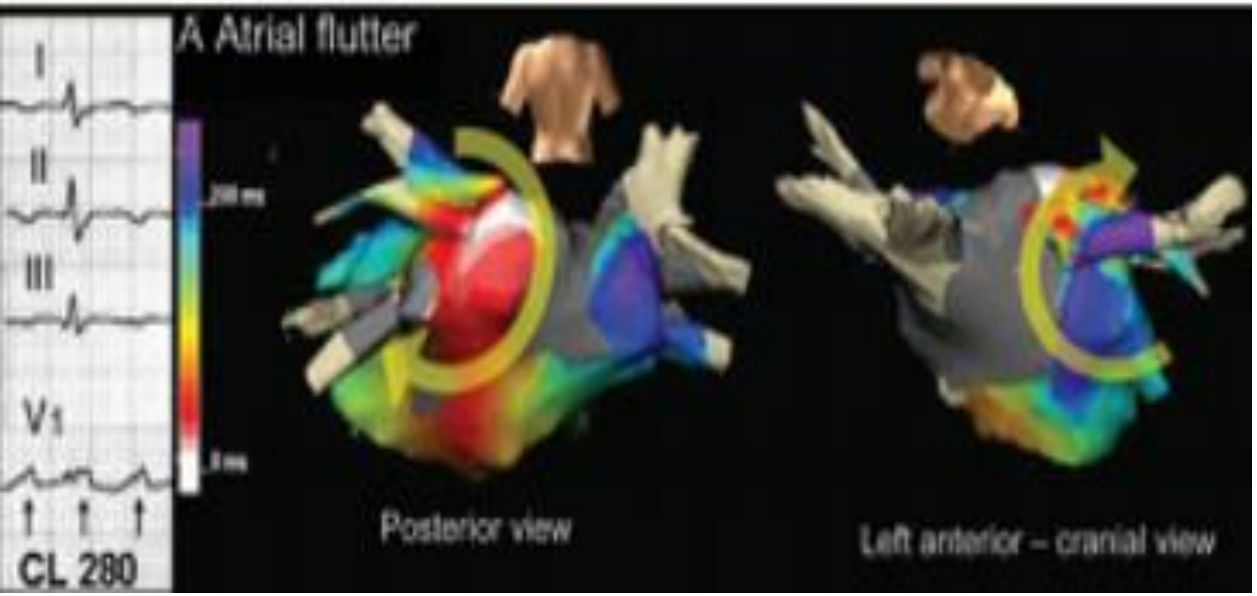
Heart viewed from the front has the tips of the right and left atrial appendages (RAA and LAA) pulled back (left). Blunt dissection reveals Bachmann's bundle (BB) crossing the interatrial groove (white arrows). The black arrows mark the rightward and leftward extensions. The blue oval marks the anticipated site of the sinus node. Longitudinal cut through the left heart (right) displays BB cut in cross-section (*). Note that it adds considerably to the thickness of the left atrial (**LA**) wall in this heart. LSPV indicates left superior pulmonary vein; RSPV, right superior pulmonary vein; and SVC, superior vena cava.

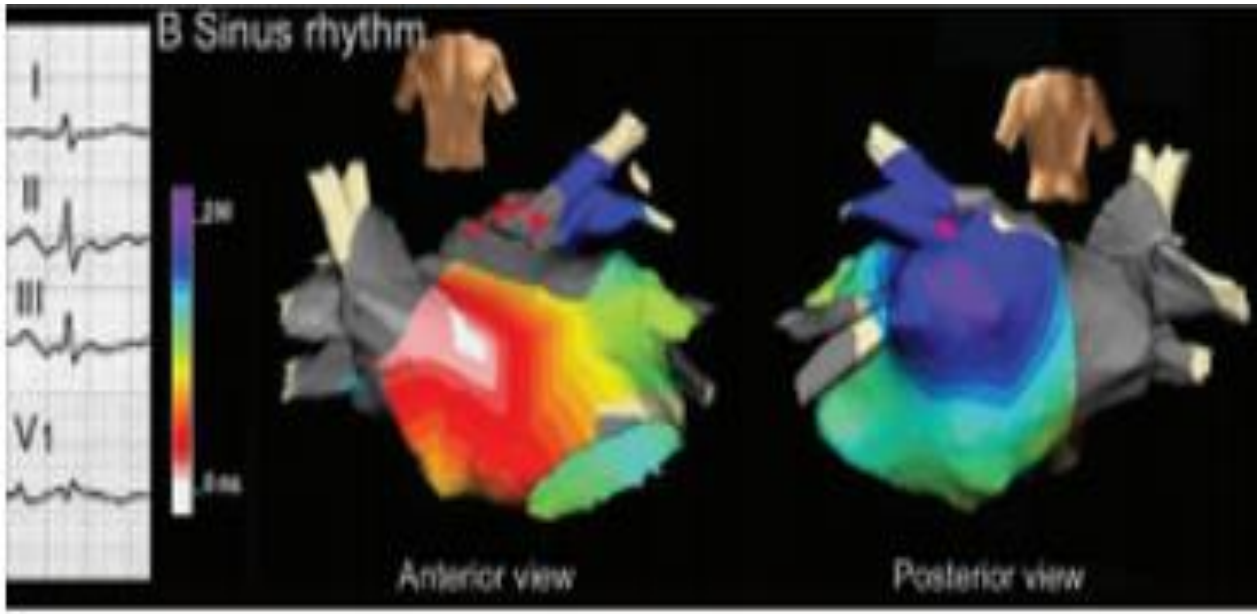


*** Epicardial fat**

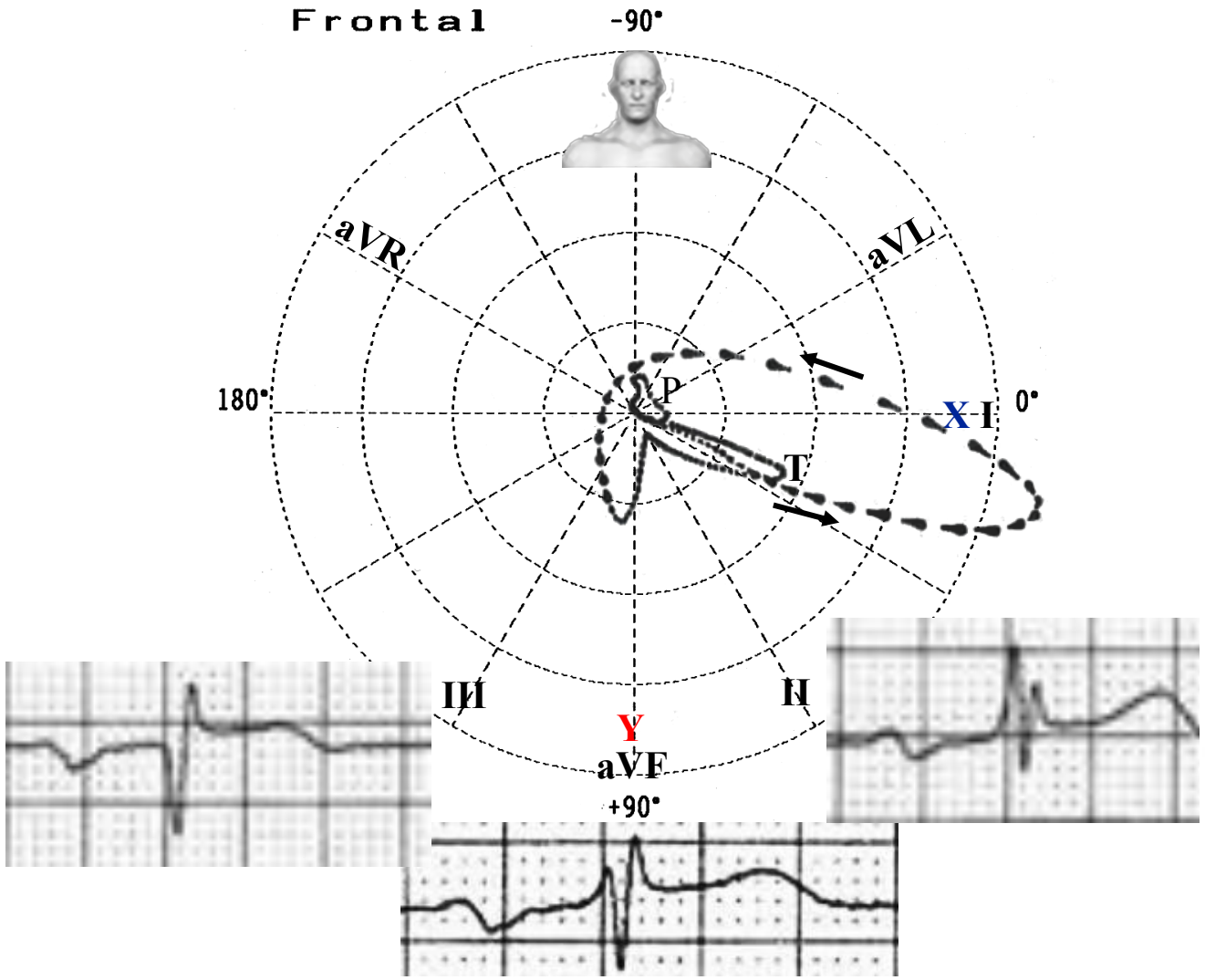
Longitudinal cut through Bachman's bundle and the atrial septum in a heart shows the bundle passing epicardial to the interatrial groove that is filled with epicardial fat (*). IVC indicates inferior vena cava; LAA, left atrial (LA) appendage; LSPV, left superior pulmonary vein; RA, right atrium; and SVC, superior vena cava.

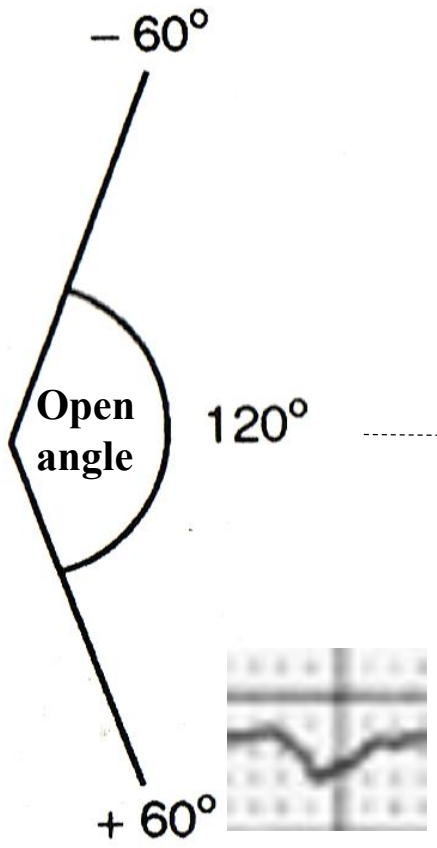
Hinojar et al postulated that BB block pattern resulting from inexcitable areas peripheral to the BB (**Hinojar 2013**). The ECG P-wave pattern, P-wave duration ≥120 ms, and bimodal plus-minus in inferior leads has been attributed to Bachmann's bundle block (BBB). Hinojar et al have mapped **LA** activation in a patient with mild mitral stenosis, displaying this pattern, and with history of recurrent atypical flutter. Failure of multiple antiarrhythmic drugs prompted an EPS with trans septal access to the **LA**. Electroanatomic map during flutter disclosed a large low-voltage area in the posterior–superior **LA** and macro-reentrant activation around the left superior pulmonary vein (LSPV). Ablation of an isthmus between the LSPV and the low-voltage area interrupted the tachycardia. ECG in sinus rhythm displayed a wide + P-wave, identical to pre-ablation recordings. **LA** activation started at the superior-septal wall (presumed insertion of BB but it was blocked along the **LA** roof and therefore, high lateral activation was delayed in an ascending pattern from the posteroinferior **LA** wall, explaining the pattern. Bachmann block pattern can be caused by non-excitable low-voltage areas peripheral to the insertion of BB in the high septal **LA**. This concept would fit well with the frequent association of the plus-minus P-wave pattern with **LA** macro-reentrant tachycardia: http://www.escardio.org/communities/EHRA/publications/ep-case-reports/ Documents/Bachmann-block-pattern.pdf

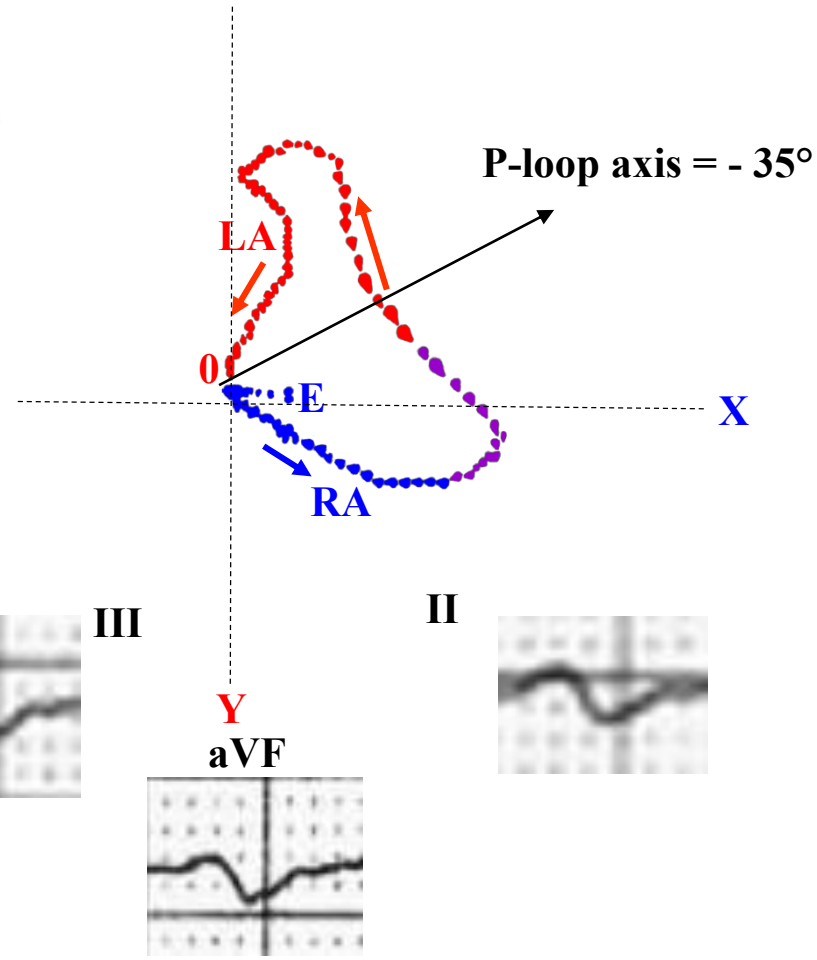




ECG/VC correlation in the frontal plane

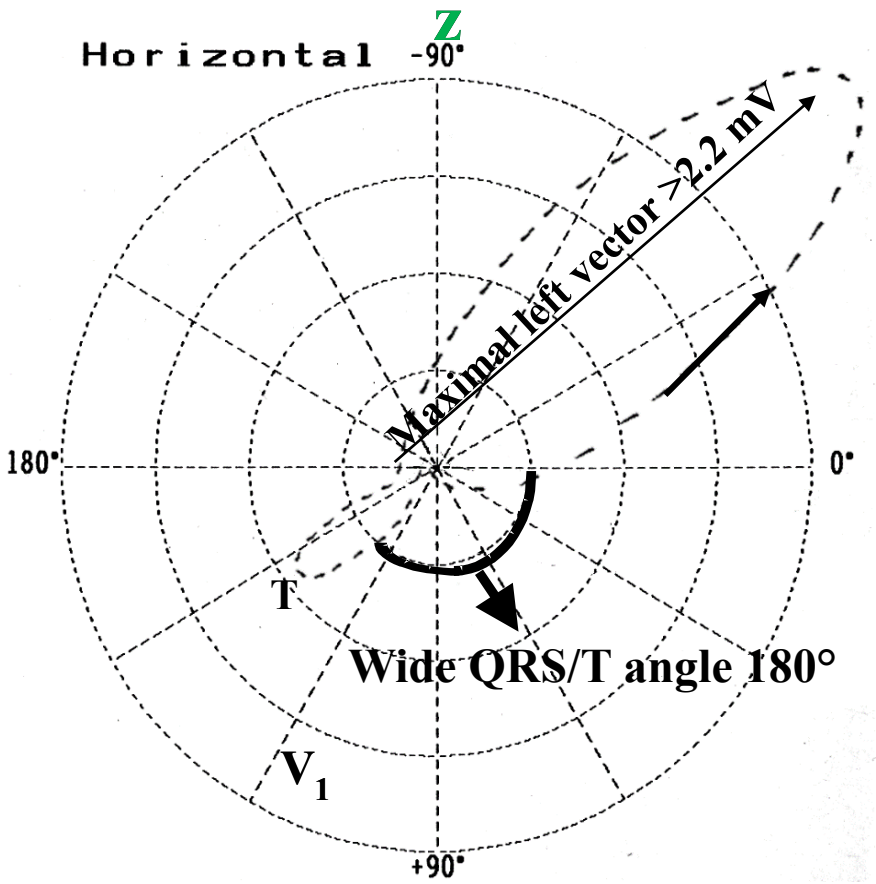




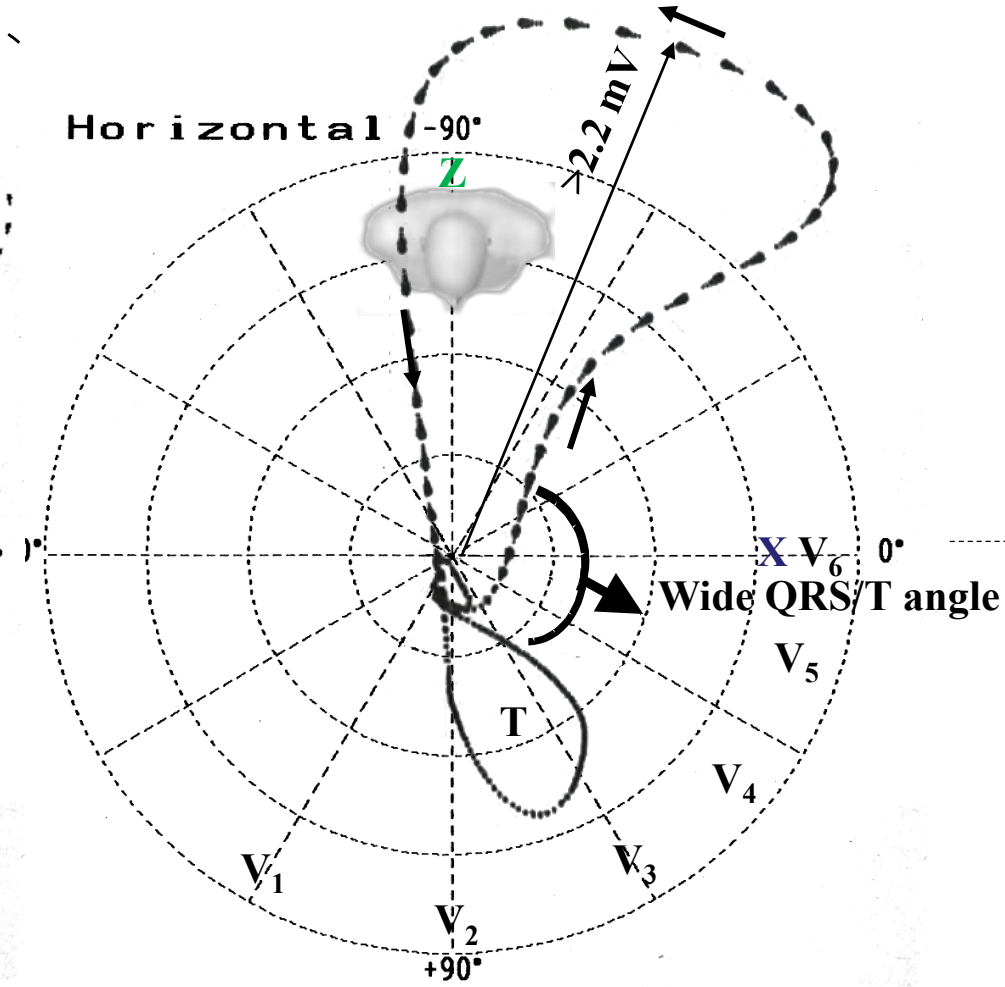


Electrical impulse is blocked/delayed in Bachmann's region muscular interatrial bundle (BB), but retrograde LA activation usually occurs.(Ariyarajah 2005) Note the existence of an open angle between the vector of the first portion of the P-wave (RA) and the last one (LA). Electrophysiological study demonstrates retrograde activation of the LA. Consequently, P loop/wave in orthogonal lead "Y", aVF and III is biphasic/positive-negative plus-minus ±. LA activation occurs by an alternate route rather than proceeding from RA to LA via the BB region.(Spodick 2007)

ECG/VC correlation in the horizontal plane



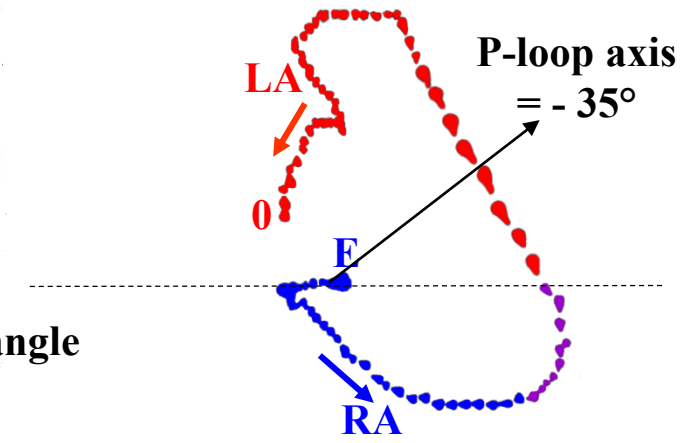
LVH with type 1A VCG



The present case

Magnified P-loop (32x)

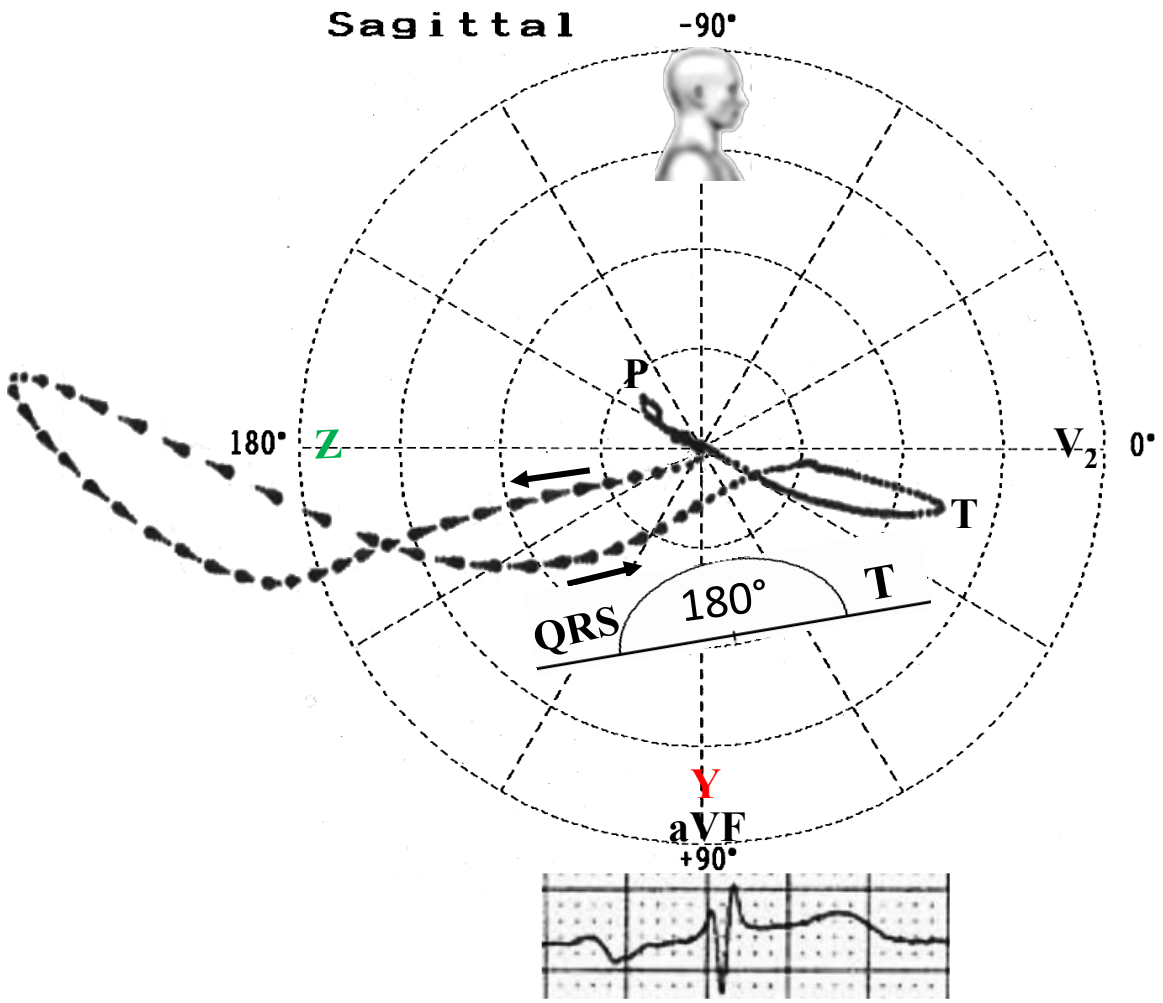
Retrograde caudo-cranial activation of the left atrium (LA)



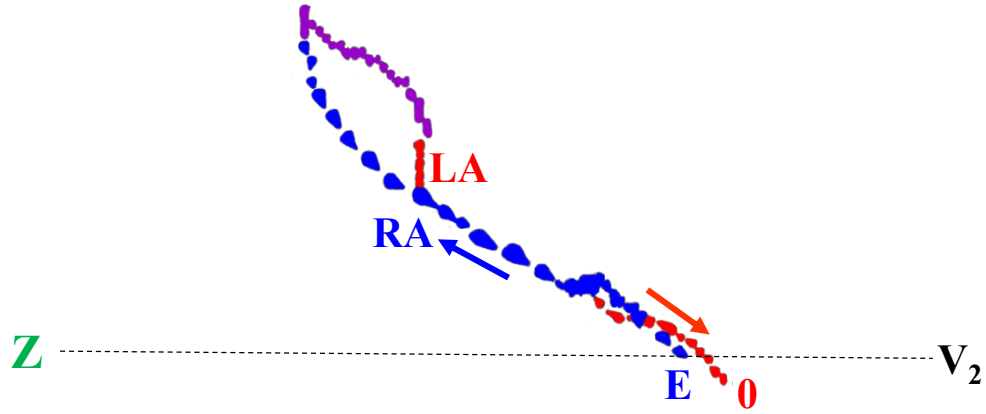
A-IAB + LAE

Instantaneous maximal left vector >2.2 mV in LVH Repolarization abnormalities: Deviation of the ST segment and the T wave in the opposite direction to the main QRS~loop causes widening QRS amplitude and wide QRS-loop /T angle (QRS/T angle near 160°):
Advanced IAB+ LAE + LVH with Left ventricular strain Pattern.

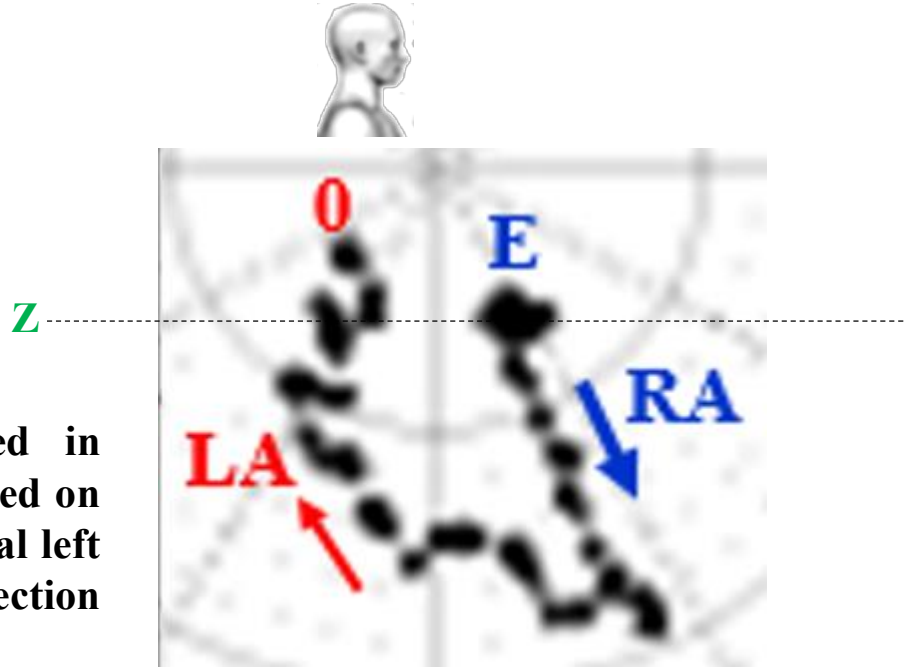
ECG/VC correlation in the Right Sagittal Plane (RSP)



Magnified P-loop (32x) in the present case

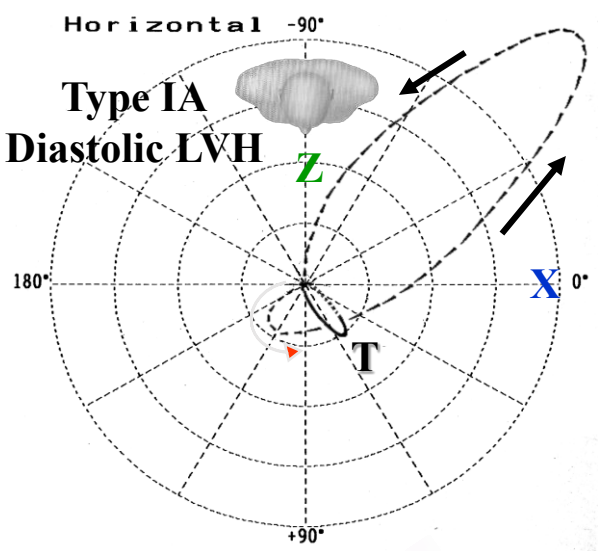


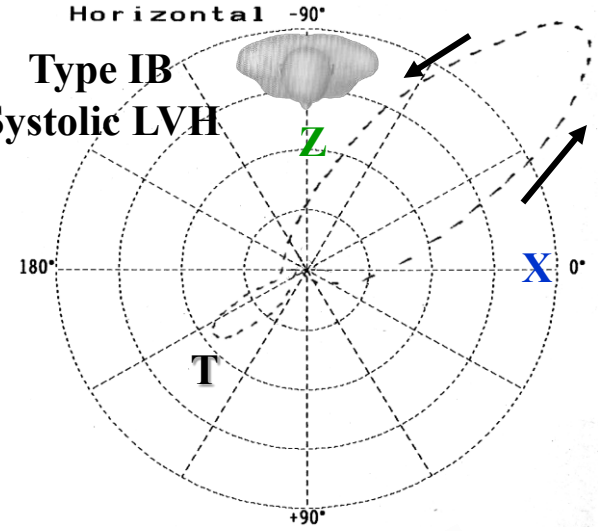
The normal magnified P-loop (32x) in the RSP

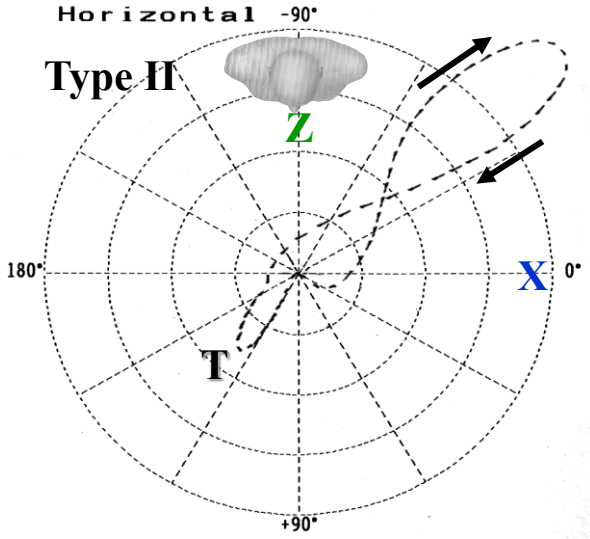


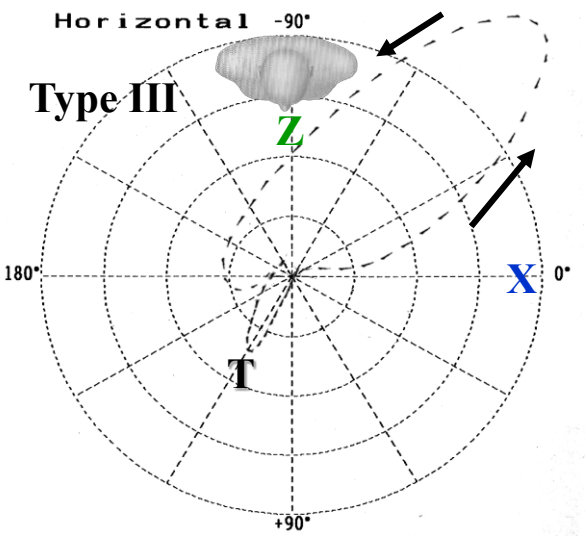
P-loop directed to back and upward (almost the entire P-loop located in posterosuperior quadrant) in RSP. In normal P wave activation P-loop is located on inferior and anterior quadrant in RSP. Plus minus P wave in aVF . The maximal left vector >2.2 mV and directed to back. QRS-loop and T-loop with opposite direction and the angle QRS/T near 180°.

The five vectorcardiographic types of LVH in the HP: IA, IB, II, III and IV



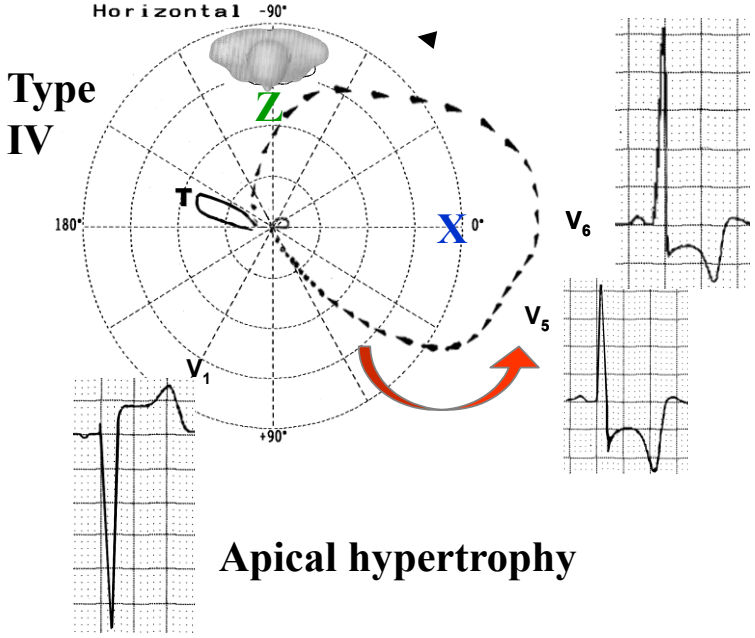






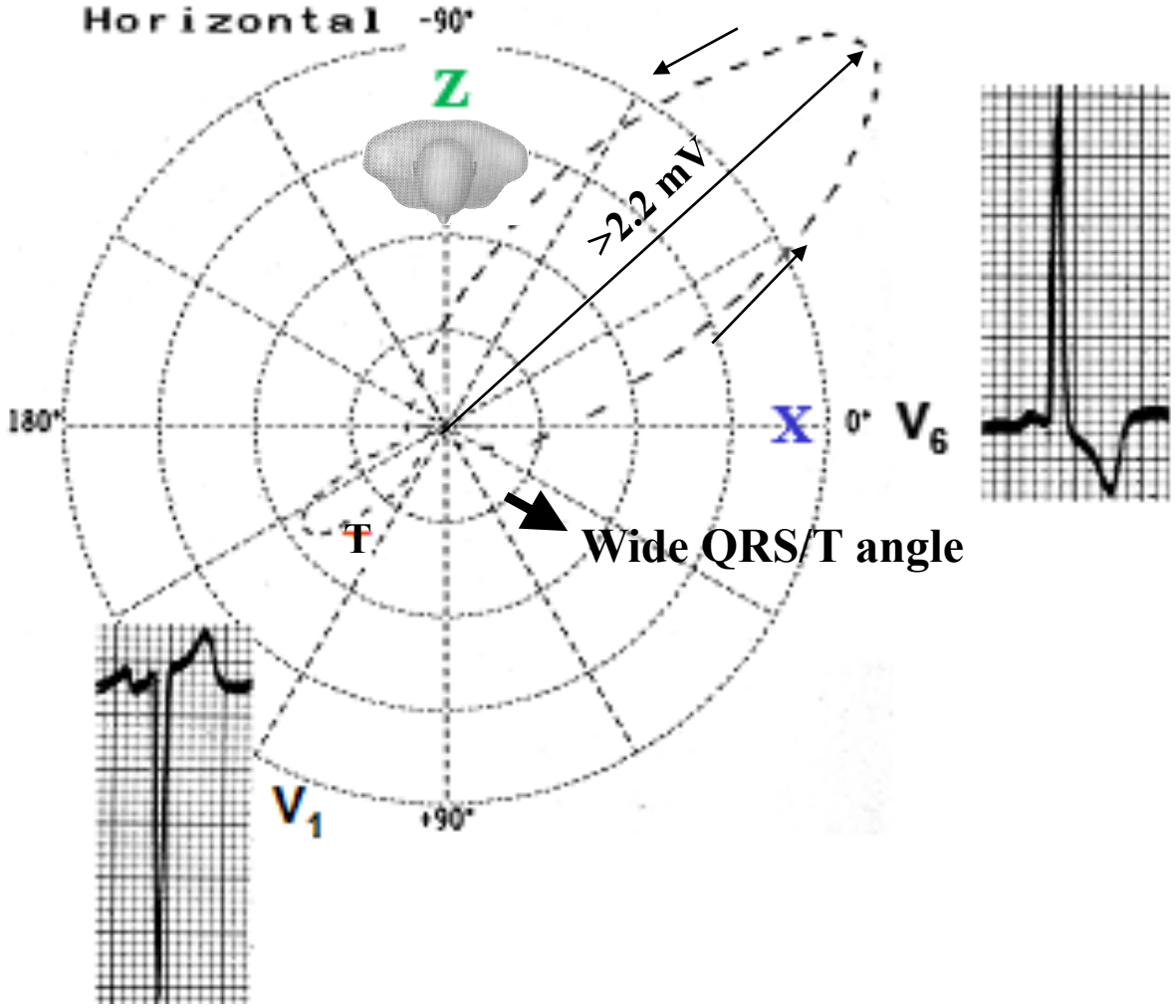
Eccentric LVH

Concentric LVH

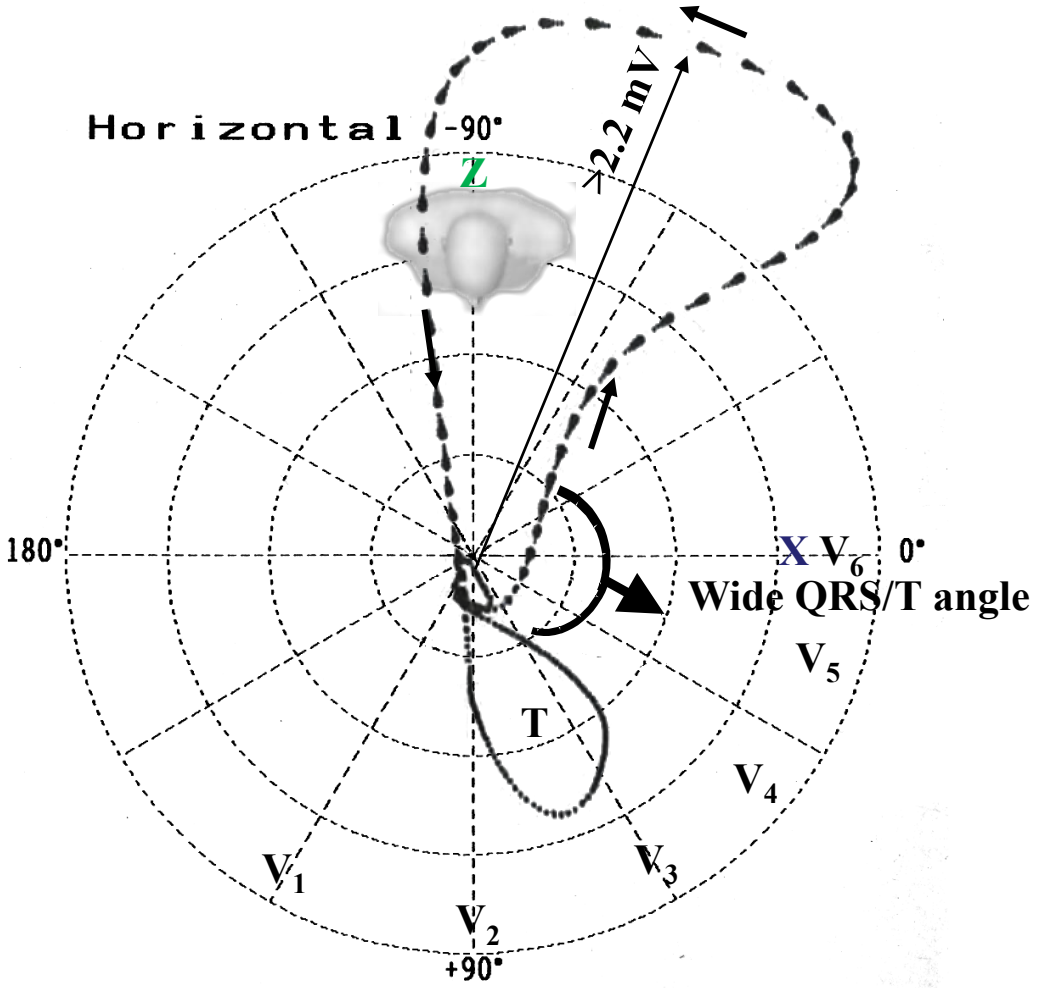


Apical hypertrophy

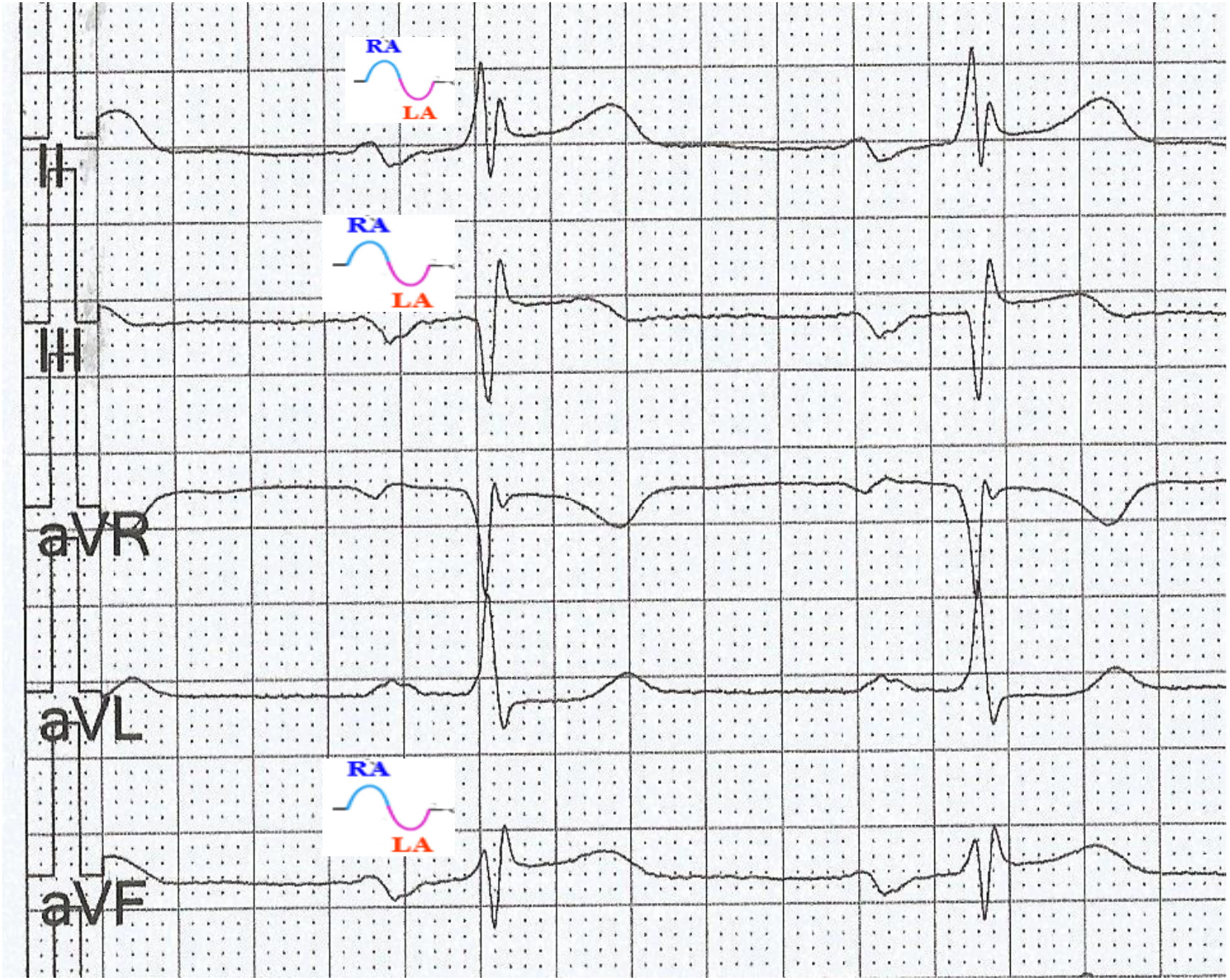
LVH Type IA vectorcardiographic

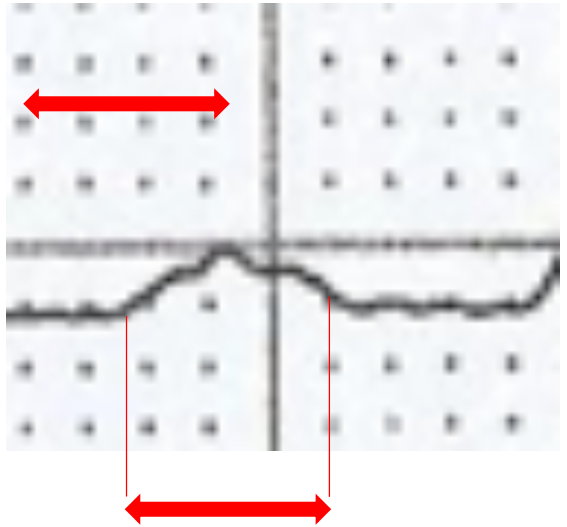


The present case: LVH Type IA vectorcardiographic



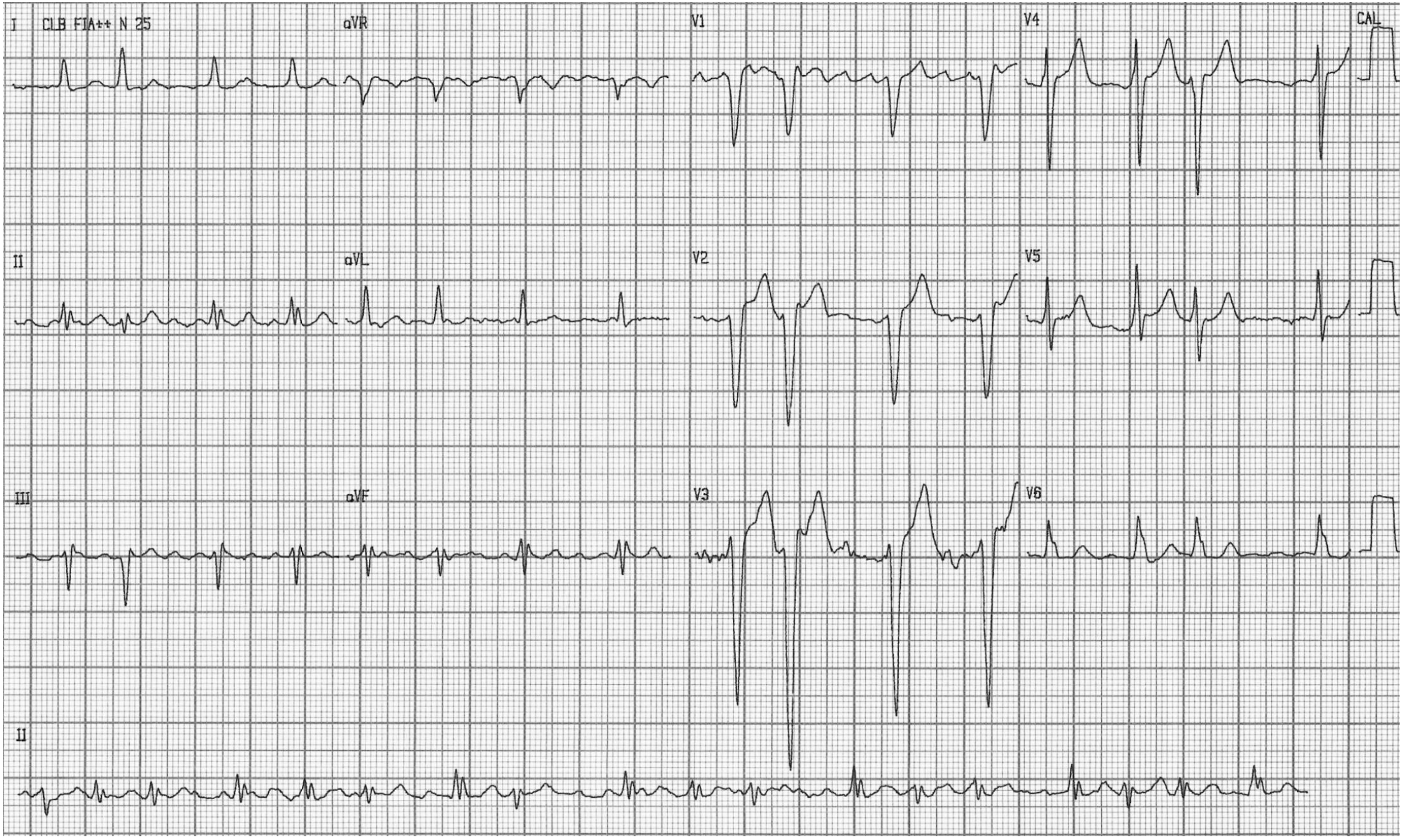
ECG and VCG with complete or advanced interatrial block + LAE





P-duration =135ms

ECG 2015



The Chronologic discoveries of a widely neglected entity: The interatrial blocks/Bayes' syndrome

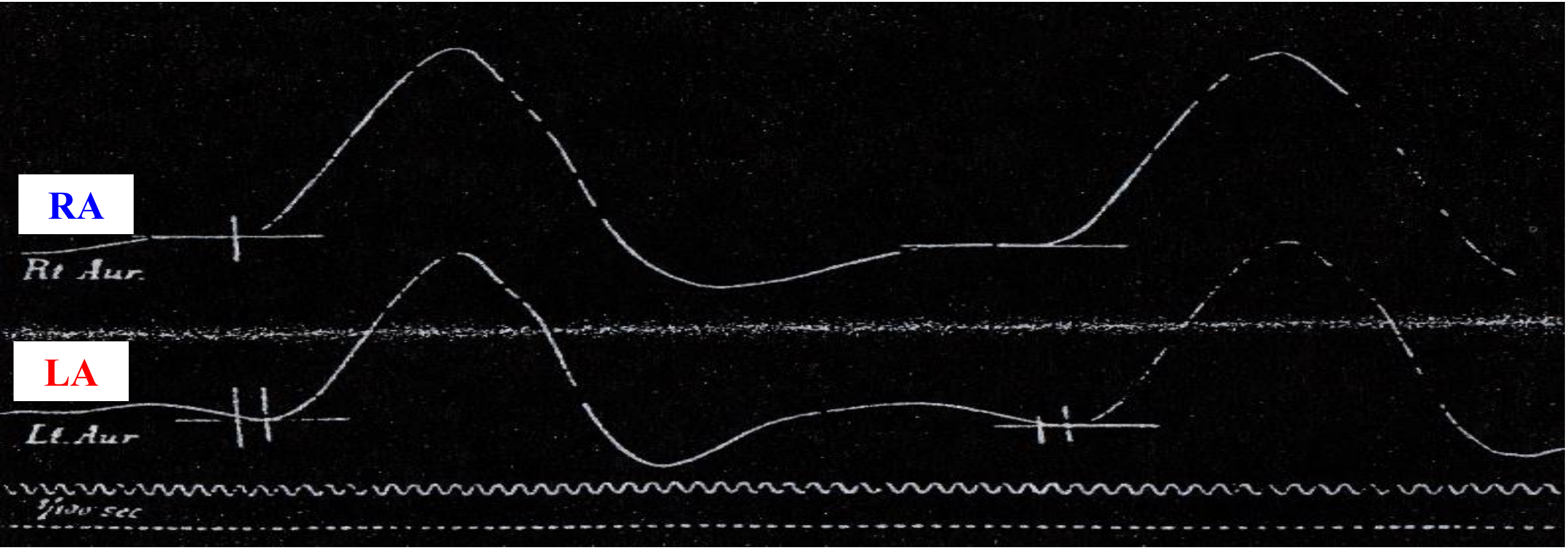
The specialized conduction band was famously known as Bachmann's bundle (BB). It is easily seen as a trapezoidal band-like structure of collimated muscle fiber coursing on the atrial walls in front of the superior vena cava and straddles the convexities of the atrial walls, connecting them in the superior quadrant of the interatrial sulcus. (**Lewis 1914**)

Jean Gorge Bachman was born on July 18, 1977, in Mulhouse in the Alsace region and grew in Nancy, France. At the age of 20, he joined the merchant marines. He made more than 20 trips across the Pacific Ocean in this service. Obviously, he was an individualist. Later he settled in the United States in 1902 where he studied medicine at Jefferson Medical College in Philadelphia, graduating in 1907 as a physician. He was professor of physiology at the Atlanta College of Physicians and Surgeons from 1910 to 1915 at Emery University School of Medicine in Atlanta from 1915 to his retirement in 1947 at the age of 70, but continued to practice medicine for several years. He died at Emory University Hospital in November 1959. He published numerous articles on cardiac electrophysiology and researched many subjects including venous pulse, arterial blood pressure measurement, and heart block. In 1934 he was one of the publishers of a physiology textbook. The Essentials of Physiology and Pharmacodynamics, published in Philadelphia. George Bachmann died in November 1959.

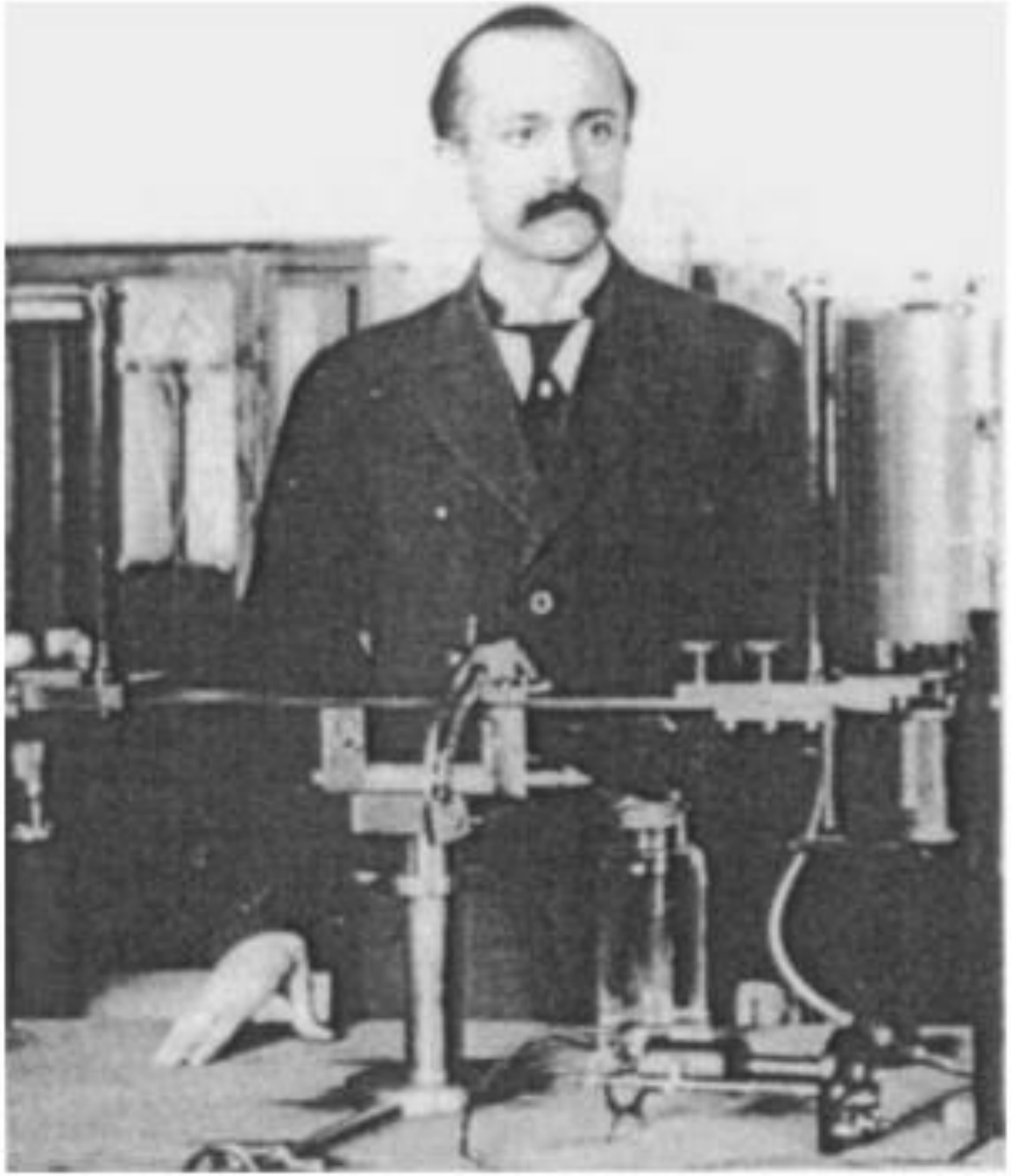
In a 1916 he wrote an article for the American Journal of Physiology entitled **“The interauricular time interval”**, Bachmann described in canine experiments the interatrial bundle, which was to be named after him, as an interatrial link allowing conduction from the right to the left atrium. The observation was made clamping the muscular bundle of fibers that connects both atria and caused a significant conduction delay (**Khaja 2005**).

The Bachmann bundle (BB) actual Bachman region or the interatrial tract is a branch of the anterior internodal tract that resides on the inner wall of the **LA**. BB represents a distinct structure similar to the atrioventricular node and the His-Purkinje conduction system but without any insulating tissue. It is a broad band of cardiac muscle that passes from the **RA**, between the superior vena cava and the ascending aorta (**James 1963**). BB is, during normal sinus rhythm, the preferential path for electrical activation of the **LA**. It is therefore considered to be part of the **"atrial conduction system"** of the heart. BB cells have specialized electrophysiological properties like supernormal excitability and faster longitudinal conduction that can facilitate more rapid impulse transmission compared to the normal atrial tissue. In BB was described bradycardia-dependent or phase 4 block (**Sobrino 1974**). These authors presented a patient with a peculiar interatrial block. The ECG showed a short PR interval and negative P waves in II, III, and aVF, which were preceded, 70ms earlier, by another positive P wave present in the right precordial leads which were absent in the limb leads. From the study with His bundle electrograms, high right atrial electrograms, and bipolar esophageal electrocardiograms, it could be proved that atrioventricular, His-Purkinje, and right intra-atrial conduction were normal, and that P-wave recorded in limb leads represented **LA** depolarization; whereas the ones in the right precordial leads corresponded to right atrial activation. The vectorial analysis from both P

waves and atrial potentials showed that the **LA** was activated in a retrograde fashion, because of an interatrial block. This block was bradycardia dependent and it disappeared in the cycles shorter than 800 ms. Experimental blockage of this pathway causes prolongation and widening of the P wave, which is associated with an increased incidence of AF. Atrial pacing is effective in reducing the incidence of AF by preventing bradycardia, synchronizing the atria, limiting anisotropy and reducing the dispersion of refractoriness. Various animal and human studies have shown pacing near the **RA** insertion of BB to have a beneficial effect in patients with interatrial conduction delay and atrial tachyarrhythmias. This mode of atrial septal pacing is convenient, safe, reliable, and clinically as effective as multisite pacing. His animal experiments to determinate the interatrial time interval mark the first time the contraction of the two atria were precisely measured. He was also able to identify the exact anatomical location of specific interatrial fibers.



Time displacement of an atrial contraction when the interatrial band is interrupted. Original Jean Gorge Bachman´s drawing.



Jean George Bachmann 1877-1959

Bachmman´s Manuscripts

1. Bachmann G: The interpretation of the venous pulse. Am JM,~~ November (1908) ri Bachniann G: C Dniplcte auriculoventricular dissnciation without S)ncopal or epileptiform attacks. Am J Med Sci 137, 342
2. Bachmann G: Sphygmographic study of a case of complete heart. block. Arch hem Med 4, 238 (1909)
3. Bachmann G: The measurement of arterial pressure in man. New Yorl Med J 93, 212 (I91)
4. Bachmann G: A physiologico-pathological study of a case of heart block occurring in a dog as a result of natural causes. J,I+,, Med XVI, I(lY12)
5. Bachmann G: An automatic spinning device for the Harvard kymo. graph. JAMA LXVI, 188 (1916)
6. Bachmann G: The inter-auricular time interval. Am J Physiol XLI, 309 (1916)
7. Bachrnann G: The distribution of the vagus nerves to the sino-auricula, junction of the mammalian heart. Am J Phgsiol LXIII, 2 (1923)
8. Bachnlann G: A Course in Erpenmenfd Physiology. Privately printed by author with illustrations by author (1924), 94
9. Bachmann G: The significance of splitting of the P-wave in thc &. Irocardiograin. Ann Infern Med 9, 14 (1941) ,
10. Haldi J: A comparative btudy of the respiratory quotient following the ingestion of glucose and of fructose as af. fected by the lactic acid and carbon dioxide changes in the bid J Nurri 2, 13 (1937)
11. Bachmann G. Haldi J, Ensor C, Wynn W: The effects of the ingestion of glucose and of fructose on the rate or excretion of urine and various constituents. Am J PhJsiol I, 12 (1938)
12. Bachmann G, Haldi J, Ensor C. Wynn W: Creatinuria following the oral administration of caffeine. Am JPhysiol I, 138 (1942)
13. Bachmann G, Haldi J, Wynn W, Ensor C: The respiratory quotient and carbohydate metabolism following the ingestion of glucose and of fructose, as affected by exercise taken immediately and 30 minutes after ingestion. Am J Phgsiol 3, I20 (1937)
14. Bachmann G, Haldi J, Wynn W, Ensor C: The effects produced b) decreasing the calcium and phosphorus intake on calcium and phosphorus absorption and disposition and on various body constituents of the rat. J Nurri 2, 20 (1Y40)
15. Haldi J, Bachmann G, Ensor C, Wynn W: Muscular efficiency In relation to the taking of food and to the height of the respirattlry quotient immediately before exercise. Am J Phgsiol I, I? (1938)
16. Haldi J, Bachinann G, Ensor C, Wynn W: Comparative effects of a high glucose and a high fructose diet on activity, body wei@ and various constituents of the liver and body of the albino exercising at will. J Nurri 3, 16 (1938)
17. Haldi J, Bachinann G, Ensor C. Wynn W: The effects on respiratory metabolism produced by equal amounts of caffeine in the form of coffee, tea, and the pure alkaloid. J Nurri 4, 27 (1944)

Chronology of the main discoveries related to interatrial blocks and Bayés´s syndrome

- **1920** Papez studied the characteristic of the atria musculature (**Papez1920**)
- **1946** Decherd et al described the interatrial and sinoatrial block, with an illustrative case.(**Decherd 1946**)
- **1956** Bradley and Marriot described the interatrial block in Circulation(**Bradley 1956**)
- **1963** Thomas described "The connecting pathways between the sinus node and A-V node and between the **RA** and the **LA** in the human heart" in the America Heart Journal. (**Thomas 1963**) In the same year, Horiba published in Japan Heart Journal the stimulus conduction in atria and in the BB with intracellular microelectrodes.(**Horiba 1963**)
- **1965** Cohen and Scherf described the atrial dissociation secondary to the complete interatrial and intra-atrial block(**Cohen 1965**)
- **1966** Wagner et al studied the specialized conducting fibers in the interatrial band published in Circulation Research. (**Wagner 1966**) The authors concluded: 1) The interatrial band is not a homogeneous structure, but contains two fiber types. 2) In addition to ordinary atrial muscle, specialized conducting fibers are present in the interatrial band. 3) Impulse spread in the interatrial band is not radial or uniform. Rather, it occurs through several linear paths which probably have infrequent cross-connections.
- **1967** De Michelis e Paparella described a case of interatrial block in Mexico.(**DeMichelis 1967**)
- **1969** Childers Merideth and Moe described for the first time supernormal phenomenon in BB in an in vitro and in vivo study in dog (**Childers 1969**). In the same year, Sanna et al described ECG features of complete interatrial block (**Sanna 1969**)
- **1970** Waldo et al . described the P wave and PR interval and the effects of the site of origin of atrial depolarization.(**Waldo 1970**) The authors studied experimentally the effects on the canine P-wave of discrete lesions in the specialized atrial tracts. In canine experiment observed that after the transection of anterior internodal tract, the P-wave duration increased significantly though morphology and polarity remained the same. However, transection of the BB not only caused increased P-duration but also distorted its polarity and morphology. (**Waldo 1970**).
- **1971** Hutter and Page presented a case of atrial arrhythmias and lipomatous hypertrophy of the cardiac interatrial septum.(**Hutter 1971**).
- **1972** Sangiorgi and Cannata described a partial interatrial block with duplex atriogram and with double atrial heterotopic, unstable interferential rhythm.(**Sangiorgi 1972**)
- **1973** Waldo et al described the etiology of prolongation of the PR interval in patients with an endocardial cushion defect. Further observations on internodal conduction and the polarity of the retrograde P wave. (**Waldo 1973**).
- **1974** Legato and Ferrer described for the fist time Intermittent or transient form of intra-atrial block its diagnosis, incidence and implications. (**Legato 1974a**). In the same year, Legato studied the atrial ultrastructure in patients with fixed intra-atrial block. (**Legato 1974b**).

- **1975:** Di Biase and Rizzon show a case of interatrial block with retrograde activation of the left atrium (**Di Biase 1975**). In this year Lee et al described "Bachmann's bundle block" associated with P mitrale in a patient with rheumatic mitral stenosis. (**Lee 1975**) and Waldo et al, showed the sequence of retrograde atrial activation in the canine heart, pointing out the correlation with positive and negative retrograde P waves. (**Waldo 1975**).
- **1976:** Zoneraich and Zoneraich studied the Intraatrial conduction disturbances and its VCGs patterns. The authors preformed the Frank P loop VCGs in 30 normal subjects and in 40 patients who had intraatrial conduction disturbances alone or in association with cardiac disease. High magnification of the P loop (0.1 mV = 3 cm) permitted accurate measurement of the P-loop duration, magnitude and direction. High-frequency recordings allowed optimal evaluation of the notches, bites and conduction delays in the PsE loop. Four VCG patterns have been selected as counterparts of the 4 types of enlarged P waves seen in ECGs of patients with atrial conduction disturbances. When intraatrial conduction disturbances coexisted with **LA** enlargement, the PsE loop was larger and smoother. The authors concluded that high magnification, high-frequency VCG of the P-loop seems to be the best available method for determining a specific pattern of intraatrial conduction disturbance.(**Zoneraich 1976**)
- **1977** Sobrino et al presented a case of bradycardia-dependent interatrial block(phase 4 block) with retrograde **LA** activation**.(Sobrino 1977)** In the same year, Leier et al showed a "dissimilar atrial rhythms" in a patient with interatrial block. The patient had type A Wolff-Parkinson-White syndrome and prolonged interatrial conduction intervals developed atrial flutter during the course of an EPS. The atrial flutter blocked along the left-to-right conduction pathways in a Wenckebach pattern. The dissimilar atrial rhythms of **RA** tachycardia and **LA** flutter evolved as the interatrial block increased to 2:1 conduction.(**Leier 1977**)
- **1979** Bayés de Luna described the block at the auricular level.(**Bayés de Luna 1979**) This is the first manuscript related interatrial blocks writhed by the great Catalonian Master. In the same year, Sherf and James described the fine structure of cells and their histologic organization within internodal pathways of the heart and its clinical and its ECG implications. (**Sherf 1979**) in 1 human and 2 canine hearts and correlated with histologic observations on more than 100 human and 10 canine hearts. From the electron microscopic studies 6 different kinds of myocardial cells were classified from two locations: the Eustachian ridge (posterior internodal pathway) and the BB (anterior internodal pathway). 5 of the 6 kinds of cells (**working myocardial cells**, **Purkinje-like cells**, either **broad or slender transitional cells** and **P cells**, and, pleomorphic and dark in appearance, with a special intertwined relation to P cells, is newly designated as an **amoeboid cell**. It was found solely in the Eustachian ridge. In the same area a rare direct contact between a nerve and a myocardial cell was observed. The authors analyzed the importance of these different kinds of cells, their respective cell connections, and their topographic locations inside the internodal pathways.

- **1981** Anderson et al studied the internodal atrial myocardium (**Anderson 1981**) The authors verified that there was nothing "special" about the myocardium between the nodes, nor was it possible to recognize tracts on the basis of either histological appearance or cellular architecture. "*From the standpoint of light microscopy, there is no evidence whatsoever to support the purported concept of specialized anatomical substrates for internodal conduction*".
- **1982** Spach et al studied experimentally in dogs the functional role of structural complexities in the propagation of depolarization in the atrium and cardiac conduction disturbances due to discontinuities of effective axial resistivity. (**Spach 1982**)
- **1983** Husson reported a case of partial interatrial block (**Husson1983**) involving the upper part of **LA**, demonstrated by esophageal recordings at different levels. Abnormally retrograde atrial depolarization in the upper part of the **LA** was observed, but normal descending depolarization in the lower part of the **LA** suggested that interatrial conduction was blocked on the BB but was normal on the middle interatrial pathway. The surface ECG showed a normal P wave duration(?); inverted P-wave in III and aVF, and flat in II an normal PR interval. The author suggests a classification of interatrial block into three types.
- **1985** Bayés de Luna et al described both ECG/VCG of interatrial blocks with **LA** retrograde activation (**Bayés de Luna 1985**) from 81,000 ECGs they collected 83 cases that fulfilled the criteria of interatrial conduction disturbances(IACD) with **LA** retrograde activation (IACD-**LARA**) (P +/- in II, III and VF with P duration ≥120 ms. The authors presented the detailed study of 35 cases with surface ECG/VCG and 29 cases with orthogonal ECG leads. The results were then compared against two control groups: with cardiopathy (30 cases) and without cardiopathy (25 cases). The prevalence of IACD-**LARA** was nearly 1% globally, and 2% among patients with valvar heart disease. The diagnostic criteria for IACD-**LARA** are:

1) ***ECG: P +/- in II, III and VF with P duration ≥120 ms***
2) ***Open angle (usually > 90°) between the first and the second part of the P-loop-wave.***
3) ***Orthogonal P +/- in Y lead (+90°-90°)with a negative mode of final> 40 ms.***
4) ***VCG: >50 ms. above the X(0°/ ± 180°) and/or Z orthogonal leads of VCG axis***
5) ***Duration of the P loop > 110 ms.***
6) ***Open angle between the two parts(initial and final) of the P loop in both frontal(FP) and right sagittal planes(RSP) (171.2° +/- 15.1), and***
7) ***Presence of notches and slurring's in the last part of the P loop.***

- **1985** Husson et al reported the case of partial interatrial block arising in the mid zone of the LA as demonstrated by esophageal recordings. These showed that atrial depolarization descending normally in the superior part of the LA was abnormally retrograde in the inferior part. This suggests a block of the mid-interatrial pathway and conduction via BB in the upper part of the LA and via a retrograde pathway in the inferior region. The surface ECG showed a P-wave of normal duration(?) which was diphasic in III and aVF with a normal PR interval. In addition, endocavitary recordings in the inferior part of the RA showed the presence of preatrial potentials during three ectopic complexes. Cause? (**Husson 1985**)
- **1987** Medrano et al. produced RA and LA damage with a subepicardial infiltration of 96° alcohol in 2 groups of dogs. In 6 other dogs the left or right portion of the interatrial band was also injured. Conventional ECG and supplementary unipolar leads were recorded using photographic and direct inscription polygraphs at paper speeds of 50 and 100 mm/s. Control, immediate postinjury and late tracings were obtained. AV block was provoked to determine QTac. Bradycardia, slight P-wave duration prolongation and PR interval were observed with both types of atrial damage. In 4 cases low RA rhythm was detected: two showed anatomohistological sinus node involvement in RA injury. Qp waves were registered over the left precordium with necrosis of both sides, but were more frequent with RA damage. Damage of the left portion of the interatrial band delayed LA activation and split P waves in the precordial leads. Damage of the RA distorts the initial vectors, magnifying the left ones and simulating LA enlargement. The Qp registered on the RA is also detected by surface leads. Contrary distorted LA depolarization increases the RA vector and delays the left, ones, giving rise to greater asynchronism and bimodal P waves.
- **1988** Bayés de Luna A et al.(**Bayés de Luna 1988**) studied 16 patients with ECG evidence of complete or advanced interatrial block(A-IAB) with retrograde activation of the LA: P duration ≥120 ms, and plus-minus (+/-) biphasic P-waves in inferior leads II, III, and VF. 8 patients had valvular heart disease, 4 had dilated cardiomyopathy and 4 had other forms of heart disease. Patients with valvular heart disease and cardiomyopathy were compared with a control group of 22 patients with similar clinical and echocardiographic characteristics, but without this type of interatrial block. Patients with A-IAB and retrograde activation of the LA had a much higher incidence of paroxysmal supraventricular tachyarrhythmias (93.7%) during follow-up than did the control group. 11 of 16 patients (68.7%) with A-IAB and retrograde activation of LA had atrial flutter (atypical in 7 cases, typical in 2 cases, and with two or more morphologies in 2 cases). 6 patients from the control group (27.7%) had sustained atrial tachyarrhythmias (5 AF and 1 typical atrial flutter). The atrial tachyarrhythmias were due more to A- IAB and retrograde activation of LA and frequent PACs than to LAE, because the control group with a LA of the same size, but without A-IAB and retrograde activation of LA and with less incidence of PACs, had a much lower incidence of paroxysmal tachycardia. In the same year, Vitali et al presented a case of interatrial block during acute myocardial infarction. **(Vitali A 1988).**

- **1989** Bayés de Luna et al.(**Bayés de Luna 1989**) demonstrated the value of preventive antiarrhythmic treatment in patients with A-IAB. In this population **LAE** is present in 90% of cases. Using drugs (amiodarone, quinidine or verapamil) this percentage was greatly lowered (25%). Atrial tachyarrhythmias such as AF and atrial flutter in advanced IAB is observed in >90% of cases. In the same year, Dolber et al studied the structure of canine Bachmann's bundle related to propagation of excitation. (Dolber1989)
- **1996** Spodick presented the relationships between interatrial block and atrial arrhythmias. (**Spodick 1996**) In the same year Ramsaran and, Spodick showed the electromechanical delay in the **LA** as a consequence of interatrial block. (**Ramsaran 1996**) **RA** and **LA** electromechanical intervals and onsets of active right and left ventricular filling were measured in patients with interatrial block and compared with control patients. The authors observed that **LA** mechanical activity is significantly delayed by interatrial block.
- **1997** Spodick DH. Wrote a revision paper about interatirla block(Spodick 1997)
- **1998** Bayes de Luna publishes a book where wrote about the interatrial blocks (**Bayes de Luna 1998**). In the same year Antz et al(**Antz 1998**) to studied experimentally the coronary sinus (CS) musculature has electrical connections to the **RA** and LA and forms an **RA**-**LA** connection. 6 excised dog hearts were perfused in a Langendorff preparation. A 20-electrode catheter (2-4-2-mm spacing center to center) was placed along the CS. Excision of the pulmonary veins provided access to the **LA**, and a second 20-electrode catheter was placed along the **LA** endocardium opposite the CS catheter. An incision opened the CS longitudinally, and microelectrodes were inserted into the CS musculature and adjacent LA myocardium. Continuous CS musculature was visible along a 35±9-mm length of the CS beginning at the ostium. During lateral **LA** pacing, CS electrodes recorded double potentials, a rounded, low-frequency potential followed by a sharp potential. The rounded initial potential propagated in the lateral-to-septal direction and represented "far-field" **LA** activation (timing coincided with adjacent **LA** potentials and with action potentials recorded from microelectrodes in adjacent **LA** cells). The sharp potential represented CS activation (timing coincided with action potentials recorded from CS musculature). A distal **LA**-CS connection (earliest sharp potential in the CS during lateral **LA** pacing) was located 26+/-7 mm from the ostium. During **RA** pacing posterior to the CS ostium, CS electrodes recorded septal-to-lateral activation of the high-frequency potential, with slightly later activation of the rounded potential (**LA** activation). Incisions surrounding the CS ostium isolating the ostium from the **RA** had no effect on the CS musculature and**LA** potentials during **RA** pacing within the isolated segment containing the CS ostium. **RA** pacing outside the isolated segment delayed activation of the CS musculature until after **LA** activation, confirming that the **RA** -CS connection was located in the region of the CS ostium as well as confirming the presence of the **LA**-CS connection.
- **2000** Parravicini et al studied the effect of M.DDD pacing and interatrial conduction block and determined the importance of optimal AV interval setting. (P**arravicini 2000**). In the same year, Harrild, and Henriquez created computer model of normal conduction in the human atria. Although considerable progress has been made in understanding the process of wavefront propagation and arrhythmogenesis in human

- atria, technical concerns and issues of patient safety have limited experimental investigations. The authors described a finite volume-based computer model of human atrial activation. The model wad three-dimensional, incorporating both the **LA** and **RA** and the major muscle bundles of the atria, including the crista terminalis, pectinate muscles, limbus of the fossa ovalis, and BB. The bundles where represented as anisotropic structures with fiber directions aligned with the bundle axes. Conductivities were assigned to the model to give realistic local conduction velocities within the bundles and bulk tissue. Results from simulations demonstrate the role of the bundles in a normal sinus rhythm and also reveal the patterns of activation in the septum. To validate the model, the simulated normal activation sequence and conduction velocities at various locations were compared with experimental observations data. The model was also used to investigate paced activation, and a mechanism of the relative lengthening of **LA** versus **RA** stimulation. Owing to both the realistic geometry and the bundle structures, the authors postulate that the model can be used for further analysis of the normal activation sequence and to examine abnormal conduction, including flutter.
- **2001** Sung et al studied the differences between conduction properties of interatrial conduits and their roles in initiation and maintenance of supraventricular arrhythmias. The objective was to determine details of interatrial activation in inferior atrial region and to correlate intra-atrial and interatrial activation patterns with the site of origin of atrial ectopic activation. In 9 dogs, basket-catheters carrying 64 electrodes were deployed into both the **RA** and **LA**. A 10-electrode catheter was inserted into the coronary sinus (CS). Activation patterns of the **RA**, **LA**, and CS were compared during pacing in the CS, in **RA** inferoparaseptum posterior to Eustachian ridge-tendon of Todaro (TT), and in inferior **RA** near the CS ostium (anterior to TT). They found that pacing in proximal and middle CS resulted in a **RA** breakthrough invariably at the CS ostium, consistent with conduction through a CS-**RA** connection. Meanwhile, **LA** breakthrough emerged in inferoposterior region (inferior to mitral annulus), suggesting conduction through a CS- **LA** connection. While pacing in distal CS, **LA** breakthrough shifted to middle posterolateral wall. Whereas, the **RA** was activated by the **LA** directly through the septum. During pacing in **RA** inferoparaseptum posterior to TT, the **LA** was activated directly through the septum at 22±4 ms. Whereas, during pacing anterior to TT, the **LA** was activated through both the CS and the septum while earliest activation was delayed by 38±5 ms. Both the interatrial septum and CS musculature form electrical conduits in inferior atrial region in canine heart. Differences in activation properties between the conduits in inferior interatrial region result in selective interatrial activation patterns during ectopic activation. (**Sung 2001**). In the same year, Roithinger et al studied the effect of the atrial pacing site on the total atrial activation time. (**Roithinger 2001**) The effect of dual site pacing for prevention of AF may be due to synchronization of **RA** and **LA** activation. 28 patients without structural heart disease were studied following RFCA of supraventricular arrhythmias. Pacing was performed using standard multipolar catheters from the presumed insertion site of BB, the CS ostium, the high lateral **RA**, and the **RA** appendage (n = 8 patients). Bipolar recording was performed from the distal CS, the high and low lateral **RA**, and the

- posterolateral **LA** (n = 13 patients). The longest conduction time from each pacing to each recording site was considered the total atrial activation time for the respective pacing site. During high RA pacing, the total atrial activation time was determined by the conduction to the distal CS (118 +/- 18 ms), during CS ostium pacing by the conduction to the high RA (94 +/- 18 ms), and during BB pacing by the conduction to the distal CS (74 +/- 18 ms). The total atrial activation time was significantly shorter during pacing from BB, as compared to pacing from other RA sites. Thus, in normal atria, pacing from the insertion of BB causes a shorter total atrial activation time and less interatrial conduction delay, as compared to pacing from other RA sites. These findings may have implications for alternative pacing sites for prevention of AF. In the same year James described the intermodal pathways of the human heart(**James2001**). In a multicenter prospective randomized study Bailin et al. compared the efficacy of Bachmann's bundle (BB) region pacing to right atrial appendage (RAA) pacing in patients with recurrent paroxysmal AF. The authors concluded that BB region pacing is safe and effective for attenuating the progression of AF.(**Bailing 2001**). Interatrial block is a strong correlate of **LAE** (enlargement) and an important predictor of supraventricular tachyarrhythmias, notably AF and flutter. It is surprising that, despite its association with arrhythmias and its effects on the electromechanical properties of the LA there is widespread neglect of this common abnormality. Jairath and Spodic investigate the prevalence of IAB in a general hospital population. They prospectively evaluated the ECGs of 1,000 consecutive adult patients. analyzed for P-wave duration. The authors showed a very high prevalence of IAB (41.1% of patients in sinus rhythm and 32.8% of all patients). It was more common in patients aged > 60 years. The authors concluded that given this unusually high prevalence of IAB in hospital patients and its ominous portents (LAE. thrombosis and embolism, arrhythmias), physicians should be aware of its frequency and computer software should be programmed to recognize it.(**Jairath 2001**). In the same year Spodick studied the of interatrial block on **LA** faction (**Spodick 2001**) and Goyal and Spodick analyzed the electromechanical dysfunction of the left atrium associated with interatrial block.(**Goyal 2001**)
- **2002** Ho et al reviews the gross structures of RA and **LA**, the septum, and the connecting great veins. They observed that the **RA** contains prominent muscular bundles and an extensive array of pectinate muscles. The distal ramifications of the terminal crest lead to the "flutter" isthmus. By contrast, the **LA** has relatively smooth walls. The atrial septum is limited to the valve of the oval fossa and its immediate muscular rim. Atrial musculature extends beyond the veno-atrial junctions to the outside of the pulmonary veins. The longest sleeves are around the upper pulmonary veins, and similar sleeves are seen around the superior cava vein. They concluded that gross structure of the atriums are more than an anatomic curiosity(**Ho 2002**). In the same year, Anderson et al studied the structure of the atriums. They observed that the **RA** is dominated by an extensive array of pectinate muscles within the extensive appendage, whereas the **LA** is relatively smooth-walled, with a much smaller tubular appendage. Myoarchitecture displays parallel alignment of fibers along distinct muscle bundles, such as the terminal crest and BB. Within the smooth wall of the **LA**, there is a marked transmural change in the orientation of the muscular fibers.

- Abrupt changes in orientation, and mixed arrangements, are common between bundles. Other than BB, the muscular bridges which provide interatrial connections, and connections between the **LA** and the CS and inferior cava vein, are highly variable. Inhomogeneities both in gross structure and myoarchitecture are common in the normal heart. These should be taken into account when investigating hearts from patients known to have had a history of arrhythmias, in devising computer models, or when refining diagnostic and therapeutic strategies. (**Anderson 2002**). Betts et al studied with three-dimensional mapping of **RA** activation during sinus rhythm and its relationship to endocardial architecture. Noncontact mapping of the **RA** was performed in 21 anesthetized swine. Isopotential and isochronal maps were superimposed upon three-dimensional reconstructions of **RA** geometry. Hearts were excised and endocardial dissection performed. Two patterns of **RA** activation were recorded. The site of earliest endocardial activation occurred either laterally at a position consistent with the terminal crest or superiorly at the junction between the superior cava vein and **RA** appendage. The subsequent spread of depolarization followed the longitudinal orientation of muscle fibers. Areas of conduction delay and block were seen at the junction between the terminal crest and posterior wall, the cavotricuspid isthmus, and around the margins of the triangle of Koch. Endocardial dissection at these sites demonstrated complex fiber orientation. A lateral site of earliest activation demonstrated a more prominent display of conduction delay or block. They concluded that the spread of the sinus impulse follows endocardial myofiber orientation and is dictated by the site of earliest activation. Even during sinus rhythm, anisotropic conduction results in areas of conduction block or delay. These findings have implications in the development of reentrant arrhythmias and may influence surgical or EPS.(**Betts 2002**). Lemery preform cardiac mapping of atrial activation with endocardial egg-shaped multiple electrodes. This approach, provided detailed assessment of the minimum number of wavelengths required to sustain AF, as well as the role of interatrial connections during AF. Subsequently, several studies on bi-atrial epicardial high-density mapping in animals and humans also reported on the importance of interatrial connections, as well as the specific characteristics of the **LA** as compared with the **RA** during chronic AF. Endocardial bi-atrial mapping studies using electrode catheters were reported using basket-shaped catheters carrying 64 electrodes. Animal studies suggested that septal activation was asynchronous and discordant, while a human study outlined the multiple origins of atrial ectopic beats following DC cardioversion in patients with chronic AF. The advent of non-fluoroscopic mapping systems significantly changed the approach to percutaneous endocardial mapping. Simultaneous bi-atrial studies using electroanatomic mapping were performed in sinus rhythm as well as in atrial flutter. These studies demonstrated the predominance of interatrial conduction over BB and the CS-**LA** connection during respectively, sinus rhythm and atrial flutter. Simultaneous bi-atrial non-contact mapping was initially performed during porcine studies and later in humans, demonstrating asynchronous and discordant septal activation both during sinus rhythm or left lateral atrial pacing. Preliminary studies from simultaneous bi-atrial non-contact mapping in humans in whom AF occurred spontaneously or was induced suggests three main types of atrial activation, consisting of **LA** drivers causing the **RA** to fibrillate following conduction over

- interatrial connections, the **RA** independently sustaining AF, even after pulmonary vein disconnection, and both atria fibrillating independently without activation over interatrial connections. Bi-atrial mapping has been essential for our understanding of normal and abnormal atrial activation, and may provide new approaches for ablation of AF.(**Lemery 2002**)
- **2003** Asad and Spodick determined the prevalence of interatrial block in a general hospital population. (**Asad 2003**) and Agarwal et al of the Spodick group researches emphasized the association of interatrial block with development of AF. **(Agarwal 2003).** Farah and Spodick studied the effect of interatrial block on coronary sinus(CS) contraction(**Farah 2003**) and Lemery et al studied the anatomic description of BB and its relation to the atrial septum. **(Lemery 2003)**
- **2004**: Spodick categorize interatrial blocks as a poorly perceived pandemic (**Spodick 2004**) In the same year Lemery et al. performed a human study of biatrial electrical coupling: determinants of endocardial septal activation and conduction over interatrial connections. The authors studied 20 patients (16 men; mean age 54±11years) with a history of symptomatic AF underwent simultaneous biatrial noncontact mapping before catheter ablation of AF. The multiple electrode array catheters were positioned, respectively, in the **LA**; transseptally and the **RA**. In all but 2 patients, isopotential maps revealed that endocardial septal activations of the **RA** and **LA** were separate, independent, and asynchronous of each other. Interatrial conduction was related to the site of initial atrial depolarization, revealing conduction over BB in all patients during sinus rhythm, high **RA** pacing, and pacing from the **LA** appendage. Pacing from the CS was associated with conduction over the interatrial connection at the level of the CS in all patients, and conduction over BB also occurred in 5 (26%) of 19 patients. Interatrial conduction over the fossa ovalis occurred in only 2 (2%) of the 116 segments analyzed. The authors concluded that electrical coupling of the **RA** and **LA** in humans is predominantly provided by muscular connections at the level of BB and the CS. The true septum (the fossa ovalis and its limbus) of the **RA** and **LA** is asynchronous and discordant, usually without contralateral conduction during sinus rhythm or atrial pacing.(**Lemery 2004**).
- **2005** Lorbar et al. emphasized the importance of the interatrial block as a predictor of embolic stroke.(**Lorbar 2005**), In the same year Ariyarajah and Spodick described "a classic ECG pattern of A-IAB". Ariyarajah et al determinate the prevalence, significance, and diagnosis of "pandemic" IAB.
- **2006** Frisella and Spodick confirm the pandemic frequency of IAB (present in 33% of hospitalized patients.) Interpreters of ECGs should seek IAB in all 12 leads since reliance on lead II alone resulted in only 53.3% of the total cases. The authors comments that the IAB with high prevalence and serious implications make necessary a more accurate recognition of this dromotropic disorder(**Frisella 2006**). In this years in successive papers Ariyarajah studied the potential clinical correlates and risk factors for IABs (**Ariyarajah a**). The progression of partial to A-IAB to atrial flutter (**Ariyarajah b**), and the prevalence of IAB in the Program of All-Inclusive Care for the Elderly (PACE (**Ariyarajah c**).

- Ariyarajah and Spodick. analyzed the BB and interatrial conduction. The BB, is considered one of its several accessory impulse-conducting pathways, plays a fundamental role in interatrial conduction. Delay in this pathway leads to P-wave duration prolongation (interatrial delay or block), which in turn is a precursor for atrial tachyarrhythmias, mainly AF and significant **LA** electromechanical dysfunction. As such, the magnitude of its sequelae has necessitated a flurry of investigations that have been targeted toward its prevention and management. Although current studies on the use of angiotensin-converting enzyme inhibitors and atrial pacing have indeed shown some promise, it would be shortsighted to overlook and circumvent the actual underlying lesion-BB abnormality. Thus, a thorough understanding of the CS and interatrial conduction is essential. (**Ariyarajah 2006 d**). In the same year Ariyarajah e al studied: 1) The optimal P-wave duration for bedside diagnosis of IAB. (e), 2) The specific ECG markers of P-wave morphology in IAB. (f) The aassociation of Duke prognostic treadmill scores with change in P-wave duration during exercise tolerance tests in patients with IAB and CHD. (g) and 4) The reevaluation of the criterion for IAB. (h) (**Ariyarajah 2006 e, f. g. h**)
- **2007** Ariyarajah et al in 4 successive papers **(Ariyarajah 2007 a;b;c;d)** analyzed: 1) the frequency of IAB in patients with sinus rhythm hospitalized for stroke and comparison to those without IAB.; 2) The association of myocardial ischemia and coronary angiographic lesions with increased **LA** dimension during exercise tolerance tests among patients without known CAD.; (c) The prospective evaluation of atrial tachyarrhythmias in patients with IABs and The IABs as novel risk factor for embolic stroke (e). In the same year, Holmqvist et al. demonstrated that The longer P-wave duration observed in HCM patients may be explained by a higher prevalence of block in one or more of the interatrial conduction routes. (**Holmqvist 2007**). Gialafos studied the prevalence of IAB in 1,353 young healthy men<35 years of age. 1,353 young healthy men. It was found that 9.1% of healthy men aged<35 years and 5.4% of those aged<20 years had P-wave durations≥110 ms. The frequent presence of IAB in leads II, V3, and V5 was also observed. Age and heart rate were independent significant determinants of IAB. The authors concluded that IAB is a frequent phenomenon, even at young ages. Thus, the early recognition of IAB might be important, possibly contributing to the prevention of future cardiovascular complications. (**Gialafos 2007**) Platonov et al analyzed that pacing studies show promising results in IABs therapy, but further studies on larger amounts of materials are required in order to identify the population of patients who would benefit more effectively from this treatment as well as the optimal pacing technique. Therefore, more extensive documentation is required before therapeutic modalities aimed at improving interatrial conduction will become a part of the clinical routine in the management of AF patients.(**Platonov 2007**)
- **2008** Spodick and Ariyarajah analyzed the IAB prevalence, and emphasized that the widely neglected, and portentous IAB (**Spodick 2008**). Loo et al observed high prevalence of widened P waves among pediatric patients in 2 separate hospitals.**(Loo 2008)**

- **2008 continuation** Ariyarajah et al observed and intermittent advanced atrial depolarization abnormality? **(Ariyarajah 2008a),** In the same year, Ariyarajah et al observed exercise-induced improvement in atrial depolarization abnormality in a patient after treatment with β-blockers**. (Ariyarajah 2008 b),** Ariyarajah et al showed the differences in echocardiographic indices between patients with partial IAB and A-IAB. **(Ariyarajah 2008 C),** Platonov et al studied the substrates for intra-atrial and interatrial conduction in the atrial septum on 84 human hearts post mortem. The atrial septum (AS), has complex structure, consequently, has been particularly difficult to study, and our knowledge of the muscular bundles providing routes for intra-atrial and interatrial conduction within the AS remains limited. The authors described the myocardial arrangement within the AS and adjacent parts of atrial walls for delineation of possible substrates for interatrial and intra-atrial conduction. They studied human heart specimens from 84 postmortem using conventional morphometric assessment, blunt dissection, and light microscopy of serial histological sections of AS. The observed that the Interatrial muscular connections are present anteriorly, posteriorly between right pulmonary veins, and inferiorly between the CS and the right inferior pulmonary vein. The inferior connections can be more prominent than the BB. Atrial musculature in the fossa ovalis consists of muscular bands isolated by fatty tissue from the endocardium of the **RA** and **LA**. They are arranged along the anterior-posterior axis and have connections with **LA** myocardium. Myocardial fascicles in the posterior-inferior and superior portions of the muscular rim of fossa ovalis originate on the **RA** side and can be traced toward the AV node. The general myocardial arrangement in the AS and adjacent regions of atrial walls are important for understanding propagation of atrial activation for selection of the optimal treatment strategy. Raja et al studied the differences in treadmill exercise tolerance parameters between patients with partial and advanced IAB. (**Raja 2008**). Baranchuk et al described a intermittent IAB after electrical cardioversion for AF. (**Baranchuk 2008**).
- **2009:** Spodick enfatize the concept of advanced , third-degree or complete IAB (**Spodick 2009**). In the same year, Ho et al emphasized the importance of knowledge of atrial structure and fibers. The general arrangement of the myofibers that make up the atrial walls was reviewed by the authors to provide a morphologic basis for atrial conduction and potential substrates of arrhythmias. The **RA**, dominated by its appendage, is characterized by having an extensive array of pectinate muscles. These extend almost perpendicularly from the terminal crest. The **LA** has relatively smooth walls and a small tubular-shaped appendage. The myofibers show changes in orientations when traced through the thickness of the walls. Extensions of atrial myocardium onto the pulmonary veins and the superior cava vein are common. Apart from BB, there are other muscular bridges of variable numbers and sizes that provide interatrial connections, connections between the **LA** and the CS, and connections between the muscular sleeves of the right pulmonary veins and the **RA**.(**Ho 2009**). Spodick et al. correlated IAB with P-terminal forces.(**Spodick 2009**). Spodick et al maintains that IABs exists in pandemic proportions in unselected hospital patients. Because of its pathologic implications it requires widespread attention which, heretofore, has been lacking. Fernandes et al. perform a preliminary observation of prospective assessment of cardiovascular events in patients with partial and advanced IAB.(**Fernandez 2009**).

- Havmöller et al studied 67 healthy volunteers (29 males, aged 63 ± 14 years, 48 females, 60 ± 13 years). Orthogonal lead data (**X**, **Y,** and **Z**) were derived from standard 12-lead ECGs (recording length 6 minutes, sampling rate 1kHz, resolution 0.625 muV) recorded at baseline (BL), and 3 years later at follow-up. P waves were then signal-averaged and analyzed regarding P-wave morphology, locations of maxima, minima, zero-crossings, and P-wave duration (PWD). They observed no differences of P-wave variables were observed at follow-up compared to BL, including PWD (127 ± 12 vs 125 ± 14 ms at BL and follow-up, respectively, n.s.). In 59 of the 67 subjects (88%), the P-wave morphology was unaltered at follow-up . However, in the remaining 8 cases a distinctively different morphology was observed. The most common change was from negative polarity to biphasic (-/+) in Lead **Z** (n=5). In one case the opposite change was observed and in two cases transition into A-IAB morphology was evident at follow-up. They concluded that In the majority of healthy subjects, P-wave morphology is stable at 3-year follow-up . Subtle morphological changes, observed principally in Lead **Z**, suggest variation of interatrial conduction. These changes could not be detected by measuring conventional PWD that remained unchanged in the total population.(**Havmöller 2009**)
- **2011:** Baranchuk studied 180 consecutive patients with obstructive sleep apnea(OSA). (**Baranchuk 2011**) They concluded that older age and moderate-severe OSA are predictors of IAB. P-wave dispersion is increased in patients with moderate-severe OSA. This may partly explain the high prevalence of atrial arrhythmias in patients with OSA. In the same year, Spodick et al studied a case with acute pericarditis superimposed on RBBB, LPFB , and IAB. (**Spodick 2011**)
- **2012:** Proietti et al observed dynamic variations of P-wave duration in a patient with acute decompensated congestive heart failure. (**Proietti 2012**). Zhao et al used a computer models that capture key features of the heterogeneous myofiber architecture of **RA** and **LA** and interatrial septum(IAS) provide a means of investigating the mechanisms responsible for atrial arrhythmia.. The aims of this study were to characterize surface geometry and myofiber architecture throughout the atrial chambers and to investigate the effects of this structure on atrial activation. Atrial surface geometry and myofiber orientations were reconstructed in 3D at 50×50×50-μm resolution from serial images acquired throughout the sheep atrial chambers. Myofiber orientations were determined by Eigen-analysis of the structure tensor. These data have been incorporated into an anatomic model that provides the first quantitative representation of myofiber architecture throughout the atrial chambers. By simulating activation on this 3D structure, they have confirmed the roles of specialized myofiber tracts such as the crista terminalis, pectinate muscles, and the BB on the spread of activation from the sinus node. They also demonstrate how the complex myocyte arrangement in the posterior **LA** contributes to activation time dispersion adjacent to the pulmonary veins and increased vulnerability to rhythm (**Zhao 2012**).

- disturbance generated by ectopic stimuli originating in the pulmonary vein sleeves. The authors developed a structurally detailed, image-based model of atrial anatomy that provides deeper understanding of the role that myocyte architecture plays in normal and abnormal atrial electric function. Chhabra et al demonstrated that IAB is a novel risk factor for acute mesenteric ischemia. (Chhabra 2012). Bayés de Luna, et al perform the first consensus to separates A-IAB from LAE (Bayés de Luna 2012).
- **2013** Hinojar et al postulated that BB block pattern resulting from inexcitable areas peripheral to the BB(Hinojar 2013) The ECG P-wave pattern, P-wave duration≥120 ms, and bimodal plus-minus in inferior leads has been attributed to Bachmann's bundle block. van Campenhout et al have mapped LA activation in a patient with mild mitral stenosis, displaying this pattern, and with history of recurrent atypical flutter. Failure of multiple antiarrhythmic drugs prompted an EPS with trans septal access to the LA. Electroanatomic map during flutter disclosed a large low-voltage area in the posterior–superior LA and macro-reentrant activation around the left superior pulmonary vein (LSPV). Ablation of an isthmus between the LSPV and the low-voltage area interrupted the tachycardia. ECG in sinus rhythm displayed a wide + P-wave, identical to pre-ablation recordings. LA activation started at the superior-septal wall (presumed insertion of BB but it was blocked along the LA roof and therefore, high lateral activation was delayed in an ascending pattern from the posteroinferior LA wall, explaining the pattern. Bachmann block pattern can be caused by non-excitable low-voltage areas peripheral to the insertion of BB in the high septal LA. This concept would fit well with the frequent association of the + - P-wave pattern with LA macro-reentrant tachycardia: http://www.escardio.org/communities/EHRA/publications/ep-case-reports/ Documents/Bachmann-block-pattern.pdf. Baranchuk et al in a letter respond to Hinojar et al (Hinojar2013) The electroanatomical mapping (CARTO) showed by Hinojar et al. in sinus rhythm shows that the atrial activation starts normally, but its propagation is blocked along the LA roof and the high lateral activation is delayed and directed caudocraneally starting at the posteroinferior LA region. Therefore, this type of atrial activation may be explained by two vectors: the first positive component of the P-wave/loop in a craneocaudal direction, and the second negative component of the P-wave/loop due to caudocraneal activation. This ECG pattern was reported several decades redefined the concept and also determined the ECG– VCG y diagnostic criteria. A very frequent association with supraventricular tachyarrhythmias (atypical flutter and AF) was also reported. The presence of atrial tachyarrhythmias in a 2-year follow-up occurs in 94% of patients with A-IAB, being atrial flutter the most frequent presentation (69% of cases), and only in 28% of the control group. This led different authors to consider that the association of A- IAB (prolonged P-wave duration + ECG pattern consisting in P-waves in leads II, III, and aVF with plus-minus pattern) with atrial arrhythmias constitutes an arrhythmological syndrome. Therefore, the case of Hinojar et al., is a clear example of the association mentioned above, and reintroduces the idea of considering antiarrhythmic treatment when this type of IAB is detected. Indeed, Baranchuck suggested this idea in a small series presented more than two decades ago. (Baranchuck 2013)

- **2013 cont…** Peyrou et al . Presented a case report of a Primary cardiac lymphoma in BB and involvement of interatrial connections between both atria across the septum. IAB (**Peyrou 2013**)
- **2014** Mehrzad and Spodick emphasized the virtual pandemic character of IAB (**Mehrzad 2014**). In the same year, Chhabra et al characterized the IAB in the modern era.The authors highlight the value of ECG and presented their approach strategies (**Chhabra 2014**). Proietti et al showed that IAB is an under-recognized ECG diagnosis with important clinical-therapeutic implications (**Proietti 2014**). Almehairi and Baranchuk presented an unusual cause of automatic mode switching in the absence of an atrial tachyarrhythmia (**Almehairi 2014**). Conde et al indicated the prevalence of IAB in patients undergoing coronary bypass graft surgery (**Conde 2014a**). Conde and Baranchuk used for the first time the eponymous Bayés syndrome for IAB as anatomical-electrical substrate for supraventricular arrhythmias (**Conde 2014b**). Enriquez et al showed A-IAB associated with recurrence of AF post pharmacological cardioversion (**Enriquez 2014a**). Huo et al showed the relationship between the P-wave characteristics and histological atrial abnormalities (**Huo 2014**). Enriquez et al emphasized the relation of IAB to new-onset AF in patients with Chagas cardiomyopathy and ICDs (**Enroquez 2014b**). Baranchuk et al clarified the concepts related P-wave duration and P-wave morphology in IAB to predict AF recurrence (**Baranchuk 2014**). Petersson et al demonstrated that the P-wave morphology is unaffected by atrial size in healthy athletes (**Peterson 2014**). Chhabra et al emphasized IAB main topics in the modern era (**Chhabra 2014**). Enriquez et al in a letter to the Editor showed that IAB and AF could be approached with invasive and noninvasive methods. They wrote that the invasive measurement offers a more definitive evidence of the real interatrial conduction time. However, it is an invasive measurement that constitutes an important limitation for its use as a clinical risk stratification tool. They noticed that Deftereos et al did not comment on the importance of the surface P-wave morphology, which, as we demonstrated, provides important information on how to stratify the risk of developing AF/atrial flutter in different clinical scenarios. When patients with partial IAB (P-wave duration <120 ms) and A-IAB (P-wave duration ≥120 ms plus-minus in leads II, III, and aVF) with similar clinical and **LA** sizes were compared, the incidence of AF/atrial flutter was found to be much higher in patients with A-IAB than in patients with partial IAB. These observations have been confirmed later by different authors in different clinical scenarios (postelectrical and pharmacological cardioversion, post–pulmonary vein isolation, and in patients with Chagas disease) by different authors. It is clear now that the presence of A-IAB in ECG is a useful marker of risk to easily and noninvasively identify patients who may need a closer follow-up. Conde and Baranchuk have recently coined a term in recognition of the one who investigated this phenomenon—Prof. Dr. Bayés de Luna—to describe the association of A-IAB with atrial arrhythmias: Bayés syndrome. (**Enriquez 2014c**).

- **2015:** Conde, Baranchuk and Bayés de Luna emphatisized tha A-IAB as a substrate of supraventricular tachyarrhythmias: a well recognized syndrome.(**Conde 2015a**). Marano et al showed that hemodialysis affects interatrial conduction (**Marano 2015**). Conde et al reinforced the concept of Bayés' syndrome as the association between A-IAB and supraventricular arrhythmias (**Conde 2015b**). Enriquez et al showed the progressive IAB and supraventricular arrhythmias (**Enriquez 2015a**). Enriquez et al demonstrated a new-onset AF after cavotricuspid isthmus ablation with identification of A-IAB as clue of the diagnosis (**Enriquez 2015b**). Baranchuk and Bayés de Luna explained the clinical significance of P-wave morphology (**Baranchuk 2015**). Sarrias et al wrote a letter to the Editor showing that IAB is another risk factor after RFCA of typical atrial flutter (**Sarrias 2015**). van Oosten and Baranchuk demonstrated that IAB is not a predictor of post-CABG AF (**van Oosten 2015**). Nielsen et al showed that the P-wave duration and the risk of AF: results from the Copenhagen ECG Study (**Nielsen 2015**). Sadiq et al showed that A-IAB predicts new onset AF in patients with severe HF and cardiac resynchronization therapy (**Sadiq 2015**). Enriquez et al presented a case of intermittent second-degree IAB in hemodialysis patients (**Enriquez 2015c**). Marano and Baranchuk demonstrated that **LA** dynamic function and IAB in hemodialysis patients (**Marano 2015**).
- **2016:** Sadiq et al showed a P-wave pseudonormalization after iatrogenic coronary sinus isolation (**Sadiq 2016**). Baranchuk, Bayés de Luna and Breithardt wrote a letter to the Editor showing the role of A-IAB pattern as a predictor of AF (**Baranchuk 2016**). Martínez-Sellés et al emphasized the incidence of A-IAB in centenarians and clinical implications (**Martinez-Sellés 2016a**). Martínez-Sellés et al discussed if we should anticoagulate patients at high risk of AF (**Martinez-Sellés 2016b**). O'Neal et al explained the ECG of A-IAB and AF risk in the general population (**O'Neal 2016**). Henmi et al discussed the concept of .interatrial conduction time and its capacity to predict new-onset AF after RFCA of isolated, typical atrial flutter (**Henmi 2016**). Gul and Baranchuk studied A-IAB as a predictor of AF following RFCA in the **LA** (**Gul 2016**). Martínez-Sellés Robledo and Baranchuk showed IAB and the risk of ischemic stroke (**Martinez-Sellés 2016c**). Britton, et al paced IAB in Bayés' Syndrome (**Britton 2016**). Alexander et al discussed the impact of A-IAB on new-onset AF following TAVR procedure (**Alexander 2016**). Martínez-Sellés, Baranchuk, Elosua and Bayés de Luna presented rationale and design of the BAYES (Interatrial Block and Yearly Events) registry (**Martinez-Sellés 2016d**). Rago et al emphasized the role of the atrial electromechanical delay in predicting AF in beta-thalassemia major patients (**Rago 2016**). Tereshchenko presented an screening entire healthcare system ECG database observing the association between deep terminal negativity of P wave in lead V1 and ECG referral with mortality (**Tereshchenko 2016**). Lacalzada-Almeida et al studied the value of speckle-tracking echocardiography in A-IAB (**Lacalzada-Almeida 2016**). Gul et al showed the IAB and interatrial septal thickness in patients with paroxysmal AF undergoing RFCA in long-term follow-up study (**Gul 2016**).
- **2017:** Barbosa-Barros et al show the first case in the literature of association between IAB and Brugada Syndrome (**Barbosa-Barros 2017**). Alexander et al compared the extent of CAD in patients with and without IAB and implications for new-onset AF (**Alexander 2017**).

- **2017 cont….** Zedda et al explained the meaning of changing P-wave morphology (**Zedda 2017**) Arboix et al showed the relationship between Bayés syndrome and acute cardioembolic ischemic stroke (**Arboix 2017**). Fernández-Fernández emphasized that AF could be caused by an underdiagnosed and easily recognizable IAB (**Fernández-Fernández 2017**). Morin et al in Reply to Fenández-Fernández wrote that IAB is an interesting ECG finding that has been reported to correlate with changes in atrial structure and function, including a shift to caudocranial left atrial activation that has been proven with VCG and electroanatomic mapping. As Dr Fernández-Fernández indicates, IAB is associated with supraventricular tachyarrhythmias including AF and atrial flutter. One of several possible conditions linking IAB with AF may be **LAE**, which is an established risk factor for AF and is found in 85% to 100% of patients with major ECG A-IAB. Thus, it is unclear whether there exists a truly causative relationship between A-IAB and AF or whether A-IAB coexists with AF simply because of their common association with **LAE**. This question, and others, may be answered by the longitudinal BAYES (IAB and Yearly Events) registry, which aims to follow 654 patients with IAB of varying severity for 3 years. Because of the unfortunate absence of routine implantable loop recorder use, the BAYES registry has suboptimal sensitivity for detecting incident AF, but it may offer insight into the risk of clinically evident AF as well as stroke risk. Examination of patients with IAB but structurally normal atria, admittedly an unusual finding, also would be of value (**Morin 2017**).

Reasons why interatrial atrial blocks are little known

1. Most of the literature studies employ only lead II or a combination of 2 or 3 leads (**Stefanadis 2001**).
2. Any of the 12 leads of the standard ECG may have the widest P waves, which establish the magnitude of block. Given the high prevalence of IAB in hospital patients and its ominous portents (LA enlargement, thrombosis and embolism, arrhythmias), physicians should be aware of its frequency and computer software should be programmed to recognize it. (**Jairath 2001**).
3. Much of the literature concerning IAB has loosely named it for one of its correlates in nearly every case; in IAB an abnormally wide P is seen on ECG and IAB should be named by its precise name.
4. ECGs encoding systems do not have a code for IAB.

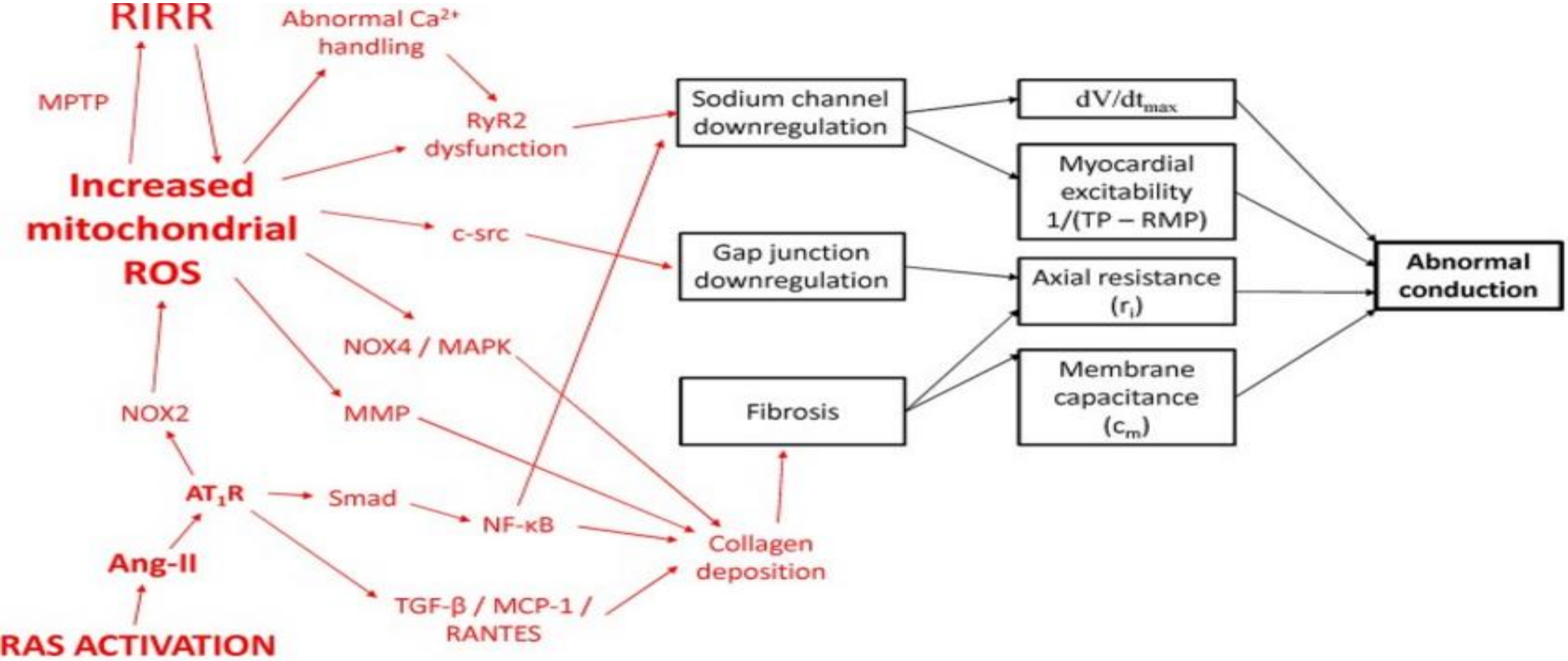
Etiology of Bayes' Syndrome (modified from Tse 2016)

1. Systemic sclerosis
2. Rheumatoid arthritis
3. Hypertrophic Cardiomyopathy such as the present case
4. Hypertensive heart disease such as the present case
5. Abnormal protein deposition in atrium amyloidosis
6. Diabetic cardiomyopathy
7. Atrial septum aneurysm
8. Atrial Septal Defects (ASDs)
9. Coronary artery disease. Conde et al indicated the prevalence of IAB in patients undergoing coronary bypass graft surgery (**Conde 2014**). Acute myocardial infarction (**Vitaly 1988**)
10. Neoplastic processes invading the inter-atrial conduction system, such as primary cardiac lymphoma in BB region and involvement of interatrial connections between both atria across the septum. IAB (**Peyrou 2013**)
11. Volume overload (transiently or intermittent (**Ariyarajah. 2008**)during, autonomic dysfunction (**Legato 1974a**) or after electrical cardioversion for AF. (**Baranchuk 2008**). Intermittent or transient second degree of IAB observed in the same ECG recording (atrial aberrancy). These P-wave patterns are due to a block because they may (a) appear transiently, (b) be without associated **LAE**, and (c) may be reproduced experimentally. (**Bayés de Luna 2012**)
12. Electrolyte disturbances (e.i from vomiting and / or diarrhea). In other patients without an obvious cause
13. Autonomic dysfunction
14. Chagas cardiomyopathy (**Enriquez 2014b**).
15. After cavotricuspid isthmus ablation (**Enriquez 2015b**).
16. Beta-thalassemia major (**Rago 2016**).

Predisposing factors

- Diabetes mellitus,
- Hypertensive heart disease,
- Hypercholesterolemia.

Potential molecular mechanisms leading to conduction abnormalities in Bayes' syndrome



RAS, renin-angiotensin system; Ang-II, angiotensin II; AT1R, angiotensin II receptor isoform 1; NOX, NADPH oxidase; MAPK, mitogen-activated protein kinase; MCP-1, monocyte chemoattractant protein-1; MMP, matrix metalloproteinase; MPTP, mitochondrial permeability transition pore; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; RANTES, Regulated on Activation, Normal T Cell Expressed and Secreted; ROS, reactive oxygen species; RIRR, ROS-induced ROS release; TGF-β, transforming growth factor-beta; RyR2, ryanodine receptor isoform 2.

Excess amount of reactive oxygen species (ROS) and P-wave duration and P-wave dispersion relationship (Pérez-Riera 2016)

In experimental and even clinical scenarios of AF extracellular fibrosis and inflammation as well as downregulation of several ion channels and gap junctions, nexus or macula communicans have been documented in atrial tissue. Both AF and cardiac heart failure (CHF) are associated with excess amount of reactive oxygen species (ROS). These can cause trigger activity type arrhythmias (early after depolarizations (EADs) and delayed after depolarizations (DADs)), reentry and potential therapeutic targets.(**Sovari 2016**) Due to triggered activity, arrhythmias are often due to problems in the ion channels in the heart muscle cells. They can also occur as a side effect of certain anti-arrhythmic drugs such as digitalis. Excess amount of ROS alters multiple cardiac ion currents: Activation of CaMKII, c-Src, and PKC may mediate several important effects of ROS on ion currents resulting in arrhythmia. ROS produces Na^+ current reduction (via PKC and c-Src, also via abnormal splicing mRNA) and reduction conduction velocity, abnormal splicing, activation of CaMKII, c-Src, and PKC are among emerging new antiarrhythmic therapeutic targets. ROS may also alter intracellular Ca^{2+} handling in a way that generates arrhythmia.

ROS may stimulate the inward L-type Ca^{2+} current (direct or via CaMKII activation facilitating after depolarization, which can facilitate EADs) with abnormal depolarization during phase 2 or phase 3. ROS is also responsible by inhibition of K+ channels I_{to}, I_{Kr}, I_{Ks} and K_{ATP} with consequent abnormal repolarization.

ROS causes adversely affected splicing of mRNA of cardiac Na^+ channels resulting in abnormal truncated cardiac Na^+ channel proteins and a reduction in normal Na^+ channels.

In the extracellular matrix ROS promotes cardiac fibrotic process (via TGF-β) with reduction in conduction velocity and impaired myocyte-myocyte coupling due to collagen deposition.

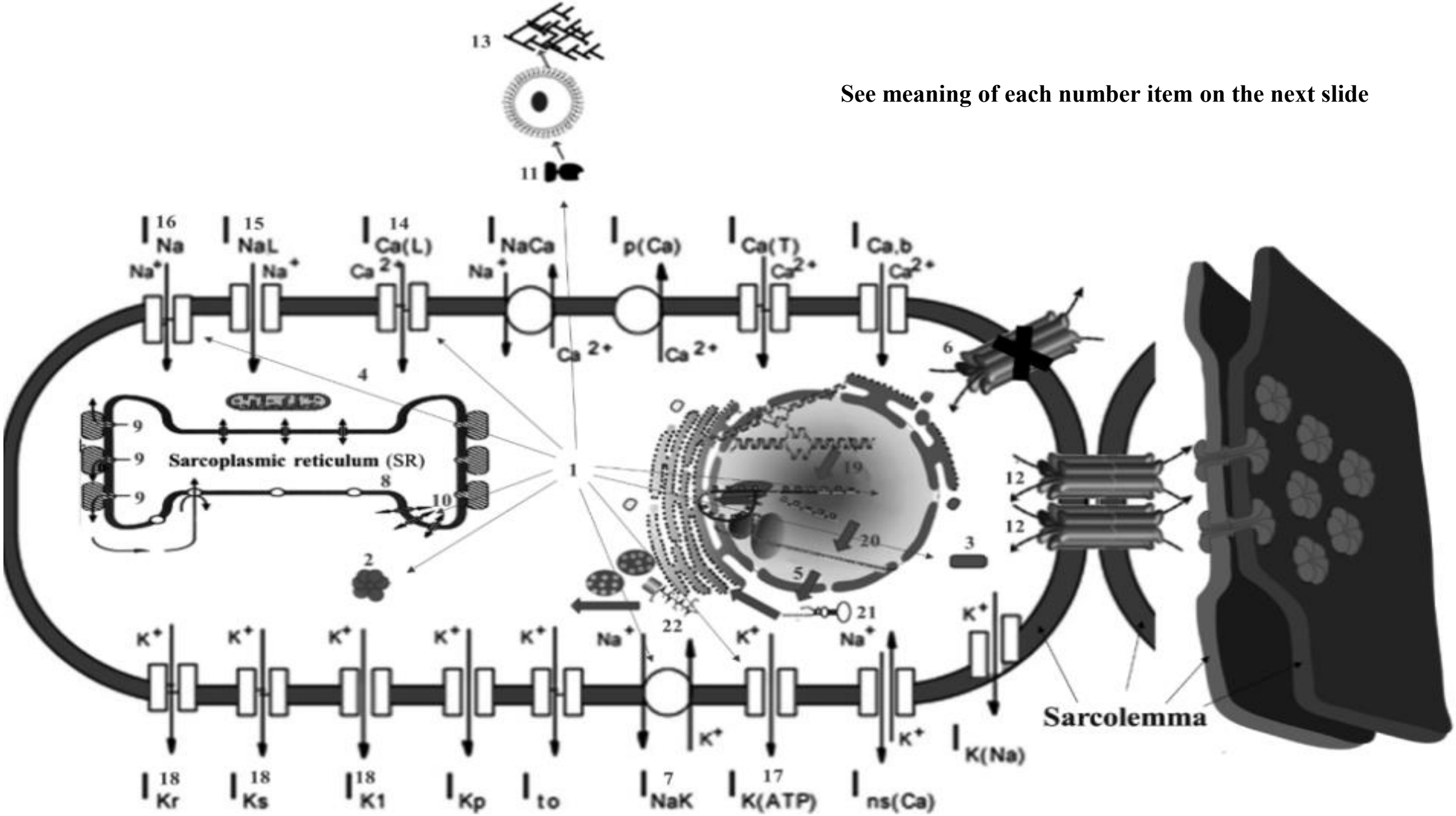
ROS impairs gap junction affecting assembling of Cx43, resulting in reduced myocyte coupling and velocity facilitation of reentry.

Activation of Ca^{2+}/CaM-dependent kinase II, c-Src tyrosine kinase, protein kinase C, and abnormal splicing of cardiac Na^+ channels are among the recently discovered molecular mechanisms of ROS-induced arrhythmia.

ROS produces NCX activation, increasing inward current afterdepolarization and increasing late Na^+ current (phase 2 of action potential) facilitating afterdepolarization. A new selective cardiac late Na^+ current inhibitor confers concurrent protection against autonomically induced atrial premature beats (APBs), and dual protection against vulnerability to ischemia-induced AF, and reduces atrial and ventricular repolarization abnormalities before and during adrenergic stimulation without negative inotropic effects.(**Justo 2016**)

In summary, ROS affects CaMKII: Ca^{2+}/calmodulin-dependent protein kinases II; CX43: connexin 43; NCX: Na^+/Ca^{2+} exchanger; PLB: phospholamban; RYR: ryanodine receptor; SERCA: sarco-/endoplasmic reticulum Ca^{2+}-ATPase; TGF-β: Transforming Growth Factor-β; ZO-1: Zonula Occludens- See next figure that shows the main action points of ROS

See meaning of each number item on the next slide



1) Excess of reactive oxygen species (ROS);
2) CaMKII activation or Ca^{2+}/calmodulin-dependent protein kinases II;
3) c-Src activation (SRC proto-oncogene, non-receptor tyrosine kinase);
4) PKC (Protein kinase C) enzymes play important roles in several signal transduction cascades. Abnormal splicing, activation of CaMKII, c-Src, and PKC are among emerging new antiarrhythmic;
5) mRNA of Na^+ current;
6) Impair gap junction CX43 conduction resulting in reduced myocyte coupling;
7) NCX: Na^+/Ca^{2+} exchanger. The NCX removes a single Ca^{2+} ion in exchange for the import of three Na^+ ions. It is considered one of the most important cellular mechanisms for removing Ca^{2+};
8) Phospholamban (PLB): It is a 52-amino acid integral membrane protein that regulates the Ca^{2+} pump in cardiac muscle and skeletal muscle cells;
9) Ryanodine receptor (RyR) participates in different signaling pathways involving Ca^{2+} release from intracellular organelles. It is the major cellular mediator of Ca^{2+} induced Ca^{2+} release (CICR) in animal cells. RyR2 is primarily expressed in myocardium;
10) Sarco-/endoplasmic reticulum Ca^{2+}-ATPase (SERCA) resides in the sarcoplasmic reticulum (SR) within myocytes. It is a Ca^{2+} ATPase that transfers Ca^{2+} from the cytosol of the cell to the lumen of the SR at the expense of ATP hydrolysis during muscle relaxation;
11) Transforming Growth Factor-β (TGF-β) leads to the activation of different downstream substrates and regulatory proteins, inducing transcription of different target genes that function in differentiation, chemotaxis, proliferation, and activation of many immune cells;
12) Zonula Occludens-1 (ZO-1) or tight junction protein. It is located on a cytoplasmic membrane surface of intercellular tight junctions. The encoded protein may be involved in signal transduction at cell–cell junctions;
13) Extracellular fibroblasts activation and collagen deposition;
14) Increase in L-type Ca^{2+} current;
15) Increase in late Na^+ current. Selective inhibition of cardiac late I_{Na} with eleclazine confers dual protection against vulnerability to ischemia-induced AF and reduces atrial and ventricular repolarization abnormalities before and during adrenergic stimulation without negative inotropic effects.
16) Na^+ current reduction;
17) ATP-sensitive K^+ channel (KATP channel) inhibition;
18) I_{to}, I_{Ks} and I_{Kr} inhibition; 19) Transcription; 20) Splicing; 21) microRNA; 22) Translation.

Treatment Options (Spodick 2004)

Reduction of interatrial block
Prevention of atrial fibrillation an other arrhythmias
Pacemaker

- Biatrial: DD pacemakers with dual atrial leads with synchronous biatrial pacing correct inter-atrial assynchrony and also prevent arrhythmia recurrence.(Dubert 1994)
- Pacing: In a multicenter prospective randomized study Bailin et al. compared the efficacy of Bachmann's bundle (BB) region pacing to right atrial appendage (**RA**A) pacing in patients with recurrent paroxysmal AF. The authors concluded that BB region pacing is safe and effective for attenuating the progression of AF.(**Bailing 2001)** Platonov et al analyzed that pacing studies show promising results in IABs therapy, but further studies on larger amounts of materials are required in order to identify the population of patients who would benefit more effectively from this treatment as well as the optimal pacing technique. Therefore, more extensive documentation is required before therapeutic modalities aimed at improving interatrial conduction will become a part of the clinical routine in the management of AF patients.(**Platonov 2007**).

  - Right atrial
  - Atrial multisite
  - Atrial septal
  - Bachmann Bundle (**Bailing 2005**) in patients undergoing coronary artery bypass surgery (CABGS). BB pacing is superior to right atrial / no pacing in the post operative period for preventing occurrence of AF and reducing intensive care unit stay, commensurate with a reduction in mean P wave duration on surface ECG.(**Chavan 1011**)
  - Ventricular.

Nonelectric approach

- Reduction of contributory comorbidities
- Myocardial failure: LV disorders; correcting these disorders may reverse the LA abnormalities.
- Inflammatory markers (e.g. high-sensitivity C-reactive protein)
- Ectopic beats
- Valve abnormalities
- Metabolic abnormalities
- Anticoagulation
- Angiotensin converting enzyme inhibition
- Angiotensin receptor blockers (**Mehrzad 2014**)
- Antiarrhythmic: Bayés de Luna et al (**Bayés de Luna 1989**) demonstrated the value of preventive antiarrhythmic treatment in patients with advanced IAB. In this population LAE is present in 90% of cases. Using drugs (amiodarone, quinidine or verapamil) this percentage was greatly lowered (25%)

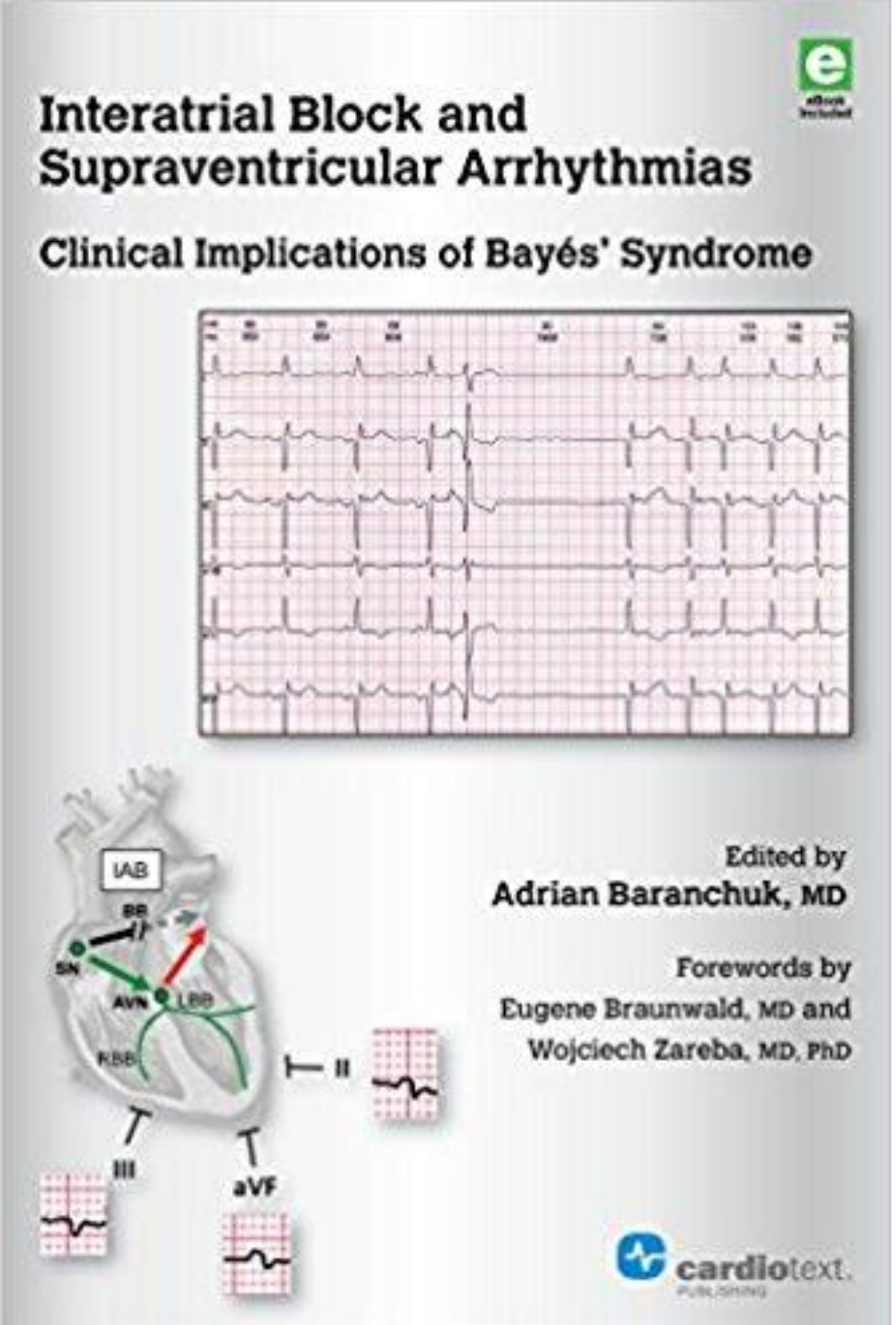
Observation: All suggested modalities should undergo appropriately designed, prospective randomized clinical trials with sufficient statistical power.

Main researchers in interatrial blocks

Jean George Bachmann (1877-1959), Nancy, France

Antonio J. Bayés de Luna (1936), Vich, near Barcelona, Spain

David H. Spodick (1927), Hartford, Connecticut, USA



Bayés syndrome refers to the association between interatrial block and supraventricular arrhythmias mainly the occurrence of atrial fibrillation. It is also a risk factor for cardio-embolic stroke. Rapid recognition by analyzing characteristic patterns in the surface ECG will help the physician to closely monitor the patient for atrial fibrillation and decide on anticoagulation therapy if the clinical risk of stroke is increased.

Interatrial blocks were described several decades ago; however, they are now gaining the attention of the medical community as a means of helping to identify patients at high risk of developing atrial fibrillation and/or cardio-embolic stroke.

I welcome all readers to navigate this book and to become familiar with this concept that is helping to renovate our models of predicting atrial fibrillation and stroke.

Foreword by Eugene Braunwald, MD:

Cardiologists are well acquainted with partial and complete blocks of conduction in the atrioventricular node, bundle of His, bundle branches, and within the ventricles. The prognostic implications and management of these blocks have been well described for decades. However, this has not been the case for blocks of interatrial conduction. While normal depolarization of the two atria and the bundle of myocardial fibers connecting them (Bachmann s bundle) were described early in the twentieth century, the recognition of blocks in interatrial conduction leading to delayed activation and contraction of the left atrium came much later, and until relatively recently have received little attention.

Professor Antoni Bayés de Luna is a distinguished and highly respected Spanish cardiologist who is widely recognized as the leading figure in contemporary clinical electrocardiography. Among his many achievements is his work on interatrial conduction blocks, which he has pursued over almost four decades. Professor Bayés has studied, investigated, described, and taught the cardiology community about this subject. In addition to providing rigorous criteria for the diagnosis and classification of the severity of these conduction blocks, he has recognized and emphasized their important association with supraventricular tachyarrhythmias. Quite appropriately, this syndrome of interatrial conduction blockade associated with these arrhythmias, most often atrial flutter or fibrillation, has been named the Bayés Syndrome.

Professor Bayés has stimulated research around the world on this syndrome. It has been learned that the syndrome occurs with increasing frequency in the elderly and may be caused by ischemia, produced most commonly by atherosclerotic obstruction of the right coronary artery, as well as by atrial distension and/or fibrosis. Importantly, the Bayés syndrome appears to be a risk factor for cardio-embolic stroke. This has raised the possibility that preventive oral anticoagulant therapy, particularly with one of the newer oral anticoagulants, might be useful in patients with advanced interatrial block, even in the absence of clinically evident atrial fibrillation.

Interatrial Block and Supraventricular Arrhythmias: Clinical Implications of Bayés Syndrome, has been superbly edited by Adrian Baranchuk, an important clinical investigator of the syndrome. Baranchuk has thoughtfully and successfully pulled together the many threads of clinical research on the syndrome. This book will surely stimulate interest in what has been a largely neglected corner of cardiology. As a consequence of the outstanding work of Bayés, Baranchuk, and the authors who have contributed to this book, interatrial block is no longer a stepchild.

Eugene Braunwald, MD

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