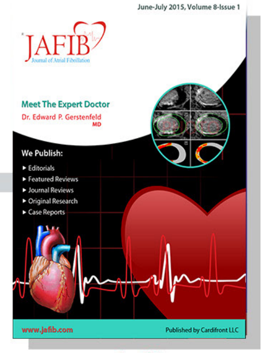
JAFIB
Journal Review
Journal of Atrial Fibrillation



www. jafib.com

Cryoablation Versus Radiofrequency Ablation in AVNRT: Same Goal, Different Strategy

Riahi Leila, Prisecaru Raluca, De Greef Yves, Stockman Dirk, Schwagten Bruno

ZNA Middelheim hospital Antwerp.

Abstract

Catheter ablation is nowadays the first therapeutic option for AVNRT, the most common benign supraventricular tachycardia. Both cryotherapy and radiofrequency energy may be used to ablate the slow pathway. This paper compares both techniques, evaluates results published in literature and gives feedback on some typical aspects of cryo- and RF ablation.

Although both techniques have satisfying success rates in AVNRT ablation, with a higher safety profile of cryoablation towards creation of inadvertent atrioventricular block, it remains paramount that the operator respects the distinctive traits of each technique in order to obtain an optimal result in every patient.

Introduction

Atrioventricular nodal re-entry tachycardia (AVNRT) is the most common benign supraventricular tachycardia.[1] The underlying substrate for the arrhythmia was first proven by Denes et al. in 1973 as being the presence of dual atrioventricular (AV) nodal pathways.[2] Although present in about 20 to 30% of people, AV nodal duality only gives rise to symptomatic tachycardia in 3% of cases.[3] Therapeutic options for symptomatic patients consist of both medical therapy and ablation. Several class I, II and IV anti-arrhythmic drugs are used to treat AVNRT. However, since the majority of patients suffering from AVNRT are in their second and third decade of life, a long-lasting drug therapy is not the most preferred option. Therefore radiofrequency (RF) ablation for AVNRT was introduced in 1982 by Gallagher et al.[4] The initial target for ablation was the fast pathway.[5] This approach soon proved to have some deleterious side effects such as complete atrioventricular block in 10%-20%[6] and so the target for ablation was moved to the slow pathway in most patients. Nowadays two options are available to ablate the slow pathway: focal cryoablation or RF ablation. Both techniques come with different advantages and disadvantages. This paper is dedicated to make a historical comparison between both techniques, evaluates results published in literature and comments on possible pitfalls in using cryo- and RF ablation.

History of Cryo- and RF Ablation

Cryoablation was initially developed in the 1970s as an alternative to surgical dissection of arrhythmic substrates.[7] Catheters for focal cryoablation are being produced since the late 1990s: for the ablation of AVNRT both a 4mm and 6mm catheter are available (Freezor and Freezor Xtra, CryoCath, Medtronic, Montreal, Canada).

One of the first papers on focal RF ablation in an animal trial was published by Scheinman et al. in 1981. They succeeded to ablate the His bundle in 9 dogs using a classic quadripolar catheter and standard direct-current (DC) defibrillator[8] thus creating rather uncontrolled myocardial damage with lesions sizing up to 4 cm. In the late 80s, the DC defibrillator was replaced by an electrosurgical generator in order to produce RF energy in a bipolar mode creating much more predictable lesions.[9] Nowadays focal RF catheters are available with 4mm, 6mm and 8mm tips.

Lesion Formation in Cryo- and RF Ablation

In order to create an effective tissue lesion using cryoablation, liquid nitrogen is pumped into the catheter and evaporates in the tip, cooling it down to less than minus 80 degrees Celsius. Before creating an irreversible lesion, the technology of cryotherapy offers the possibility of cryomapping. During cryomapping the cryocatheter tip is cooled down minus 30 degrees celsius for a maximum of 60 seconds, creating a fully reversible lesion with both a 4mm or a 6mm cryocatheter.[10] This 'test-freeze' allows the operator to safely check if ablation at the desired location will be both effective and/or safe. Efficacy can be tested during cryomapping either by using pacing manoeuvres to check for disappearance of conduction over the slow pathway or by inability to induce tachycardia by pacing or by stopping of tachycardia if the application was done during ongoing AVNRT. Safety is guaranteed since creation of any kind of atrioventricular (AV) block during cryomapping is fully reversible {Jensen-Urstad, 2006 #11).

Another advantage of cryoablation is cryoadhesion. Because of

Disclosures:
None.

Corresponding Author:
Dr. Schwagten Bruno,
ZNA Middelheim,
dienst Cardiologie,
Lindendreef 1, 2020 Antwerpen.

the ice formation, the cryocatheter tip adheres to the myocardial tissue during ablation. This adhesion avoids catheter dislodgement and unwanted cooling of the compact AV node. It allows for pacing manoeuvres during ablation without the risk of catheter dislodgement, and minor patient movements will not result in displacement of the catheter.

Cryoablation induced permanent lesion formation on the cellular level is characterized by three phases:

(1) the freeze/thaw phase,

(2) the haemorrhagic and inflammatory phase, and

(3) the replacement of this acute lesion by fibrosis. In the first phase, intracellular and extracellular ice crystals are formed with variable size. Ice crystals formed more closely to the catheter tip are intra- and extracellular, in contrast to more peripheral ice crystals, which tend to appear only in the extracellular space. During the thawing phase, mitochondria develop irreversible damage due to increased membrane permeability. The second phase, occurring within the first 48 h, is characterized by the development of haemorrhage, oedema, and inflammation. After 1 week, a sharply demarcated lesion is formed. The final phase of lesion formation takes place within 2–4 weeks. At this time, the lesion consists of dense collagen and is infiltrated by fatty tissue. In summary, consecutive freezing, inflammation, and fibrosis, leading to tissue with intact extracellular matrix, form cryolesions. The advantage of preserving the endothelium is a decreased risk of thromboembolism. A theoretical advantage could be that cryolesions are less proarrhythmic as the lesion border is more homogeneous. In contrast to extension of lesion size after stopping of RF delivery, the extent of ablated tissue does not increase anymore after the acute lesion is formed with cryotherapy {Schwagten, #12}.

RF energy induces thermal lesion formation both through resistive

Table 1: Results of literature comparing RF and Cryoablation in AVNRT using 4mm and 6mm cryocatheters

4mm tip cryoablation catheters									
	Years	**Patients (n)**		**Procedure Time (minutes)**			**Fluoroscopy Times(minutes)**		
		Cryo	**RF**	**Cryo**	**RF**		**Cryo**	**RF**	
Kimman	2004	30	33	142	144	NS	29	35	NS
Zrenner	2004	100	100	148 ±46	122±31	<0,001	12	14	<0,001
Collins	2006	57	60	148 ±46	112±31	<0,001	20 ±13	21 ±15	NS
Schwagten	2011	150	124	146±60	138±71	NS	19±15	27±22	<0,01
	Initialsuccess(%)			**Recurrence(%)**			**AVB post RF**		
	Cryo	**RF**		**Cryo**	**RF**				
Kimman	94	94	NS	10	9	NS	0		
Zrenner	97	98	NS	8	1	NS	0		
Collins	95	100	NS	8	2	NS	0		
Schwagten	96,5	96	NS	11	5	NS	2		
6mm tip cryoablation catheters									
	Years	**Patients (n)**		**Procedure Time (minutes)**			**Fluoroscopy Times(minutes)**		
		Cryo	**RF**	**Cryo**	**RF**		**Cryo**	**RF**	
Chan	2009	80	80	150	159	NS	19±11	26±17	<0,01
Opel	2010	123	149	90(45-220)	90(45-220)	NS	16(7-48)	14(5-50)	<0,05
Deisenhofer	2010	251	258	140±56	122±44	<0,001	14±8	13±8	NS
	Initial success (%)			**Recurrence (%)**			**AVB post RF**		
	Cryo	**RF**		**Cryo**	**RF**				
Chan	97,5	95	NS	9	1,3	<0,04	0		
Opel	93	95	NS	17	7	0,02	1		
Deisenhofer	96,8	98,4	NS	9,4	4,4	<0,03	1		
4 and 6mm									
	Years	**Patients (n)**		**Procedure Time (minutes)**			**Fluoroscopy Times(minutes)**		
		Cryo	**RF**	**Cryo**	**RF**		**Cryo**	**RF**	
Gupta	2006	71	71	96(60-180)	90(60-180)	NS	17 ±12	13±13	NS
Avari	2008	38	42	176(97-324)	174(68-443)	NS	19 (6-49)	21(4-158)	NS
	Initial success (%)			**Recurrence (%)**			**AVB post RF**		
	Cryo	**RF**		**Cryo**	**RF**				
Gupta	85	97	<0.05	19,8	5,6	0,01	1		
Avari	97	95	NS	2	2	NS	1		

Legends : Cryo : cryoablation, RF : radiofrequency ablation. AVB : atrioventricular nodal block after ablation. AVB after Cryo is always zero and conductive heating of myocardial tissue. The quality of the thermal injury is dependent upon both time and temperature. Tissue temperatures of 50°C or higher are necessary to create irreversible myocardial injury.[11] The central zone of the ablation lesion reaches high temperatures and is simply coagulated. Lower temperatures are reached during the ablation in the border zones of the lesion. The ultra structural appearance of the acute RF lesion shows marked disruption in cellular architecture characterized by dissolution of lipid membranes and inactivation of all structural proteins. The band of tissue, 2 to 5 mm from the edge of the pathologic lesion, manifests significant abnormalities, but despite this ultrastructural disarray, the myocytes appear to be viable in this zone.[11] After 4 to 5 days, the border between the RF lesion and surrounding tissue becomes sharply demarcated. By 8 weeks after ablation, the necrotic zone is replaced with fatty tissue, cartilage, and fibrosis and is surrounded by chronic inflammation.[12]

Results of Literature

Recently, numerous studies evaluated safety and efficacy of cryoablation compared to RF ablation in AVNRT treatment (Table I).

For the acute success, almost all studies agree on the efficacy of both types of energy with a comparable success rate ranging between 93% and 100%. Gupta et al. is the only group reporting a significant lower acute success rate using cryoablation energy (85% vs 97%, p<0,05). Regarding the long term follow up, 4 out of the 9 studies comparing RF to cryoablation showed a higher recurrence rate to be present in the cryoablation groups.

On the other hand, cryoablation is the safer technique compared to RF ablation regarding occurrence of inadvertent permanent AV block necessitating a pacemaker implantation. To our knowledge, no case of permanent AV block has been reported after cryoablation for AVNRT.

Procedure time is significantly longer using cryoablation in 3 studies. Two out of those 3 studies report the use of a 4 mm cryoablation catheter. Conversely, fluoroscopy times are longer in patients undergoing RF ablation in these trials.

Table 2: Comparison between cryoablation and RF ablation in AVNRT on different essential topics

	RF ABLATION	CRYOABLATION
Procedure duration	Shorter	Longer
Fluoroscopy	Longer	Shorter
Procedural success: long term results	97-100%	93-95%
Inadvertent AVB	1%	None reported
Junctional rhythm during ablation	Sensitive marker of success	Abscent and not related to success
Ablation during tachycardia	Risk of catheter dislodgement	Cryomapping safely possible
Acceptable procedural end point	Anterograde jump with single echo	No anterograde jump
Ablation lesion characteristics	Brush lesion	Focal lesion
Lesion extention beyond ablation	Possible (up to several months)	None
Theoretical thrombogenity of lesion	Higher	Lower
Catheter characteristics	Multiple curves available	One curve
Catheter stability	Operator dependent	Absolute (cryoadhesion)
Energy titration	Possible – operator dependent	Mandatory

Success Rates

Judging by results of literature, both energy sources prove to have a comparable acute success rate. However, cryoablation in AVNRT seems to have a slightly higher recurrence rate in the long term (Table 2).

Some suggest that catheter tip size might influence ablation outcomes in cryoablation. When 4mm and 6mm cryocatheters were still commonly used, Rivard et al published a paper obviously favouring the use of a 6mm catheter in AVNRT.[13] However more recently a meta-analysis by Hanninen et al. could not find any correlation between acute and long term outcomes and catheter size.[14]

Regarding procedural endpoints, unlike with RF, the persistence of dual AV nodal physiology after cryoablation with or without echo beats is associated with a higher long-term recurrence.[15] This might be an indication that the procedural endpoint should be more strict when using cryoablation energy. The difference in lesion size could explain the before mentioned: brush lesions created by focal RF ablation tend to be larger in surface than the focused cryolesions.

In line with these brush lesions, fluoroscopy use is significantly higher when RF is used.[14] Catheter instability due to lack of adhesion and imminent catheter dislodgement by tachycardia or pain induced patient movement can explain those results, making cryoadhesion a major advantage of ablation. Nevertheless, during cryoablation procedures, this short fluoroscopy time is counterbalanced by a longer total procedure time compared with RF,[14] as the targeting of the slow pathway must be done much more precisely with a relatively bulky catheter.

Complications

Occurrence of ablation induced permanent complete AV block using RF energy remains a major concern especially in young patients. In highly experienced centres, the incidence of permanent AV block necessitating pacemaker implantation has been reported to be about 1%.[16] Undesired ablation of the critical part of the compact AV node almost always occurs during the procedure, but evolution to a delayed total AV block can also take place even several months after the ablation procedure.[17] Initiation of a fast junctional tachycardia during ablation with loss of ventriculo-atrial (VA) conduction is associated with an increased risk of inadvertent AV block with a positive predictive value of 19%.[18] The risk of total AV block can even be predicted before RF ablation is started, using the interval between the atrial EGM on the His catheter and the atrial EGM on the distal dipole of the ablation catheter: the shorter this interval, the higher the risk of inadvertent AV block with a cut-off of 17+/- 8 ms.[19] Using Cryoablation on the other hand, to our knowledge no persistent total AV block has been described during AVNRT ablation or thereafter.

Pediatrics

AVNRT is the second most common SVT after atrioventricular re-entry tachycardia (AVRT) in children. Unlike RF catheter ablation, cryoablation holds no risk of creating permanent AV block. This is the main reason why cryoablation is the therapy of choice in this specific population. Additionally, on a cellular level, an ablation lesion created by cryoenergy leaves the exoskeleton of the cells undamaged and has a smaller surface, thus creating less destruction in these still growing hearts and avoiding jeopardizing their future. On the other hand, navigating these large and relatively stiff 6mm cryocatheters in these small hearts with even smaller triangles of Koch can be challenging. Luckily, cryomapping will help in selecting the best ablation target on the slow pathway and cryoadhesion offers absolute catheter stability during ablation in sinus rhythm, during pacing or during tachycardia. A safe and feasible way to improve success rates with cryotherapy even more in children can be the effectuation of more than one cryoablation on the slow pathway and/or by prolonging the ablation duration.[20] Interestingly, early intervention (< 12 years of age) using cryotherapy for AVNRT seems to be more efficient than later intervention.[21]

Waiting Period

Although respecting a waiting period following successful slow pathway ablation is commonly used, its effect to increase the long-term success rates still remains a subject of debate. When observing firm ablation endpoints such as non-inducibility of AVNRT, disappearance of anterograde jump and absence of echo beats, data in RF ablation for AVNRT exist, suggesting that an abbreviated procedure will result in a similar favourable outcome as a procedure including a 30 minutes waiting period.[22]

Energy Titration

In contrast to cryoablation, where the only variable to define the lesion size by the operator is the freezing time, RF ablation allows more parameters to be titrated in order to create an successful lesion.

When cyroenergy is used, a steady state in lesion size is attained between three and five minutes of therapy.[23] Some groups suggest using a freeze-thaw-freeze sequence to improve lesion quality based on results of research on hepatic tissue showing creation of deeper lesions when cryoenergy is applied as such.[24]

When RF energy is used, both temperature and power setting can be adjusted in order to effectively ablate the slow pathway. Where some operators go for direct application of full temperature and power, others favour gradual power titration. This customized approach for AVNRT treatment was first described by Langberg et al.[25] Albenque et al describe an ablation protocol with initial settings of 5W and 60 degrees and then slowly increasing the power by steps of 5W for every 5 seconds until slow-accelerated junctional rhythm is obtained, then the power is further increased to 10 W maximum above this value. In their series this results in a safer profile with only 0. 2% of permanent AV block at the cost of higher recurrence rate of 3.6%.[26,1-29]

Results

Continuous data are expressed as mean and interquartile range, while categorical variables are expressed as a percentage. Statistical analysis was performed using the program IBM® SPSS® Statistics 20 version

Conclusion

Both cryo- and RF ablation have comparable and satisfying success rates in AVNRT ablation. Historically cryoablation seems to have s slightly higher recurrence rate during long term follow-up: in order to improve these results, it is paramount to respect firm ablation endpoints. Risk of creating inadvertent AV block remains a major issue in using RF energy, thus making it less suitable to be used in young and physically active patients.

References

1. Kastor JA, Goldreyer BN, Josephson ME, et al. Electrophysiologic characteristics of Ebstein's anomaly of the tricuspid valve. Circulation 1975;52:987-95.
2. Denes P, Wu D, Dhingra RC, Chuquimia R, Rosen KM. Demonstration of dual A-V nodal pathways in patients with paroxysmal supraventricular tachycardia. Circulation 1973;48:549-55.
3. McCanta AC, Collins KK, Schaffer MS. Incidental dual atrioventricular nodal physiology in children and adolescents: clinical follow-up and implications. Pacing Clin Electrophysiol;33:1528-32.
4. Gallagher JJ, Svenson RH, Kasell JH, et al. Catheter technique for closed-chest ablation of the atrioventricular conduction system. N Engl J Med 1982;306:194-200.
5. Langberg JJ, Chin MC, Rosenqvist M, et al. Catheter ablation of the atrioventricular junction with radiofrequency energy. Circulation 1989;80:1527-35.
6. Epstein LM, Scheinman MM, Langberg JJ, Chilson D, Goldberg HR, Griffin JC. Percutaneous catheter modification of the atrioventricular node. A potential cure for atrioventricular nodal reentrant tachycardia. Circulation 1989;80:757-68.
7. Norrell HA, Winternitz WW, Wilson CB, Maddy JA. Stereotaxic cryosurgery in the management of acromegaly. Int Surg 1970;53:5-10.
8. Gonzalez R, Scheinman M, Margaretten W, Rubinstein M. Closed-chest electrode-catheter technique for His bundle ablation in dogs. Am J Physiol 1981;241:H283-7.
9. Huang SK, Bharati S, Graham AR, Lev M, Marcus FI, Odell RC. Closed chest catheter desiccation of the atrioventricular junction using radiofrequency energy--a new method of catheter ablation. J Am Coll Cardiol 1987;9:349-58.
10. Dubuc M, Roy D, Thibault B, et al. Transvenous catheter ice mapping and cryoablation of the atrioventricular node in dogs. Pacing Clin Electrophysiol 1999;22:1488-98.
11. Nath S, Redick JA, Whayne JG, Haines DE. Ultrastructural observations in the myocardium beyond the region of acute coagulation necrosis following radiofrequency catheter ablation. J Cardiovasc Electrophysiol 1994;5:838-45.
12. Huang SK, Bharati S, Lev M, Marcus FI. Electrophysiologic and histologic observations of chronic atrioventricular block induced by closed-chest catheter desiccation with radiofrequency energy. Pacing Clin Electrophysiol 1987;10:805-16.
13. Rivard L, Dubuc M, Guerra PG, et al. Cryoablation outcomes for AV nodal reentrant tachycardia comparing 4-mm versus 6-mm electrode-tip catheters. Heart Rhythm 2008;5:230-4.
14. Hanninen M, Yeung-Lai-Wah N, Massel D, et al. Cryoablation versus RF ablation for AVNRT: A meta-analysis and systematic review. J Cardiovasc Electrophysiol;24:1354-60.
15. de Sisti A, Tonet J. Cryoablation of atrioventricular nodal reentrant tachycardia: a clinical review. Pacing Clin Electrophysiol;35:233-40.
16. Calkins H, Yong P, Miller JM, et al. Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction: final results of a prospective, multicenter clinical trial. The Atakr Multicenter Investigators Group. Circulation 1999;99:262-70.
17. Kimman GP, van Hemel NM, Jessurun ER, et al. Comparison of late results of surgical or radiofrequency catheter modification of the atrioventricular node for atrioventricular nodal reentrant tachycardia. Eur Heart J 1999;20:527-34.
18. Lipscomb KJ, Zaidi AM, Fitzpatrick AP, Lefroy D. Slow pathway modification for atrioventricular node re-entrant tachycardia: fast junctional tachycardia predicts adverse prognosis. Heart 2001;85:44-7.
19. Hintringer F, Hartikainen J, Davies DW, et al. Prediction of atrioventricular block during radiofrequency ablation of the slow pathway of the atrioventricular node. Circulation 1995;92:3490-6.
20. Qureshi MY, Ratnasamy C, Sokoloski M, Young ML. Low recurrence rate in treating atrioventricular nodal reentrant tachycardia with triple freeze-thaw cycles. Pacing Clin Electrophysiol;36:279-85.
21. Drago F, Placidi S, Righi D, et al. Cryoablation of AVNRT in children and adolescents: early intervention leads to a better outcome. J Cardiovasc Electrophysiol;25:398-403.

22. Steven D, Rostock T, Hoffmann BA, et al. Favorable outcome using an abbreviated procedure for catheter ablation of AVNRT: results from a prospective randomized trial. J Cardiovasc Electrophysiol 2009;20:522-5.
23. Holman WL, Kirklin JK, Anderson PG, Pacifico AD. Variation in cryolesion penetration due to probe size and tissue thermal conductivity. Ann Thorac Surg 1992;53:123-6.
24. Theuns DA, Kimman GP, Szili-Torok T, Res JC, Jordaens LJ. Ice mapping during cryothermal ablation of accessory pathways in WPW: the role of the temperature time constant. Europace 2004;6:116-22.
25. Langberg JJ, Leon A, Borganelli M, et al. A randomized, prospective comparison of anterior and posterior approaches to radiofrequency catheter ablation of atrioventricular nodal reentry tachycardia. Circulation 1993;87:1551-6.
26. Bortone A, Boveda S, Jandaud S, et al. Gradual power titration using radiofrequency energy: a safe method for slow-pathway ablation in the setting of atrioventricular nodal re-entrant tachycardia. Europace 2009;11:178-83.
27. Jensen-Urstad M, Tabrizi F, Kenneback G, Wredlert C, Klang C, Insulander P. High success rate with cryomapping and cryoablation of atrioventricular nodal reentrytachycardia. Pacing Clin Electrophysiol 2006;29:487-9.
28. Schwagten B, Van Belle Y, Jordaens L. Cryoablation: how to improve results in atrioventricular nodal reentrant tachycardia ablation? Europace;12:1522-5.
29. Whayne JG, Nath S, Haines DE. Microwave catheter ablation of myocardium in vitro. Assessment of the characteristics of tissue heating and injury. Circulation 1994;89:2390-5.