## Original Article

# Surgical Treatment of Chronic Atrial Fibrillation —Unipolar Radiofrequency Ablation versus Cryoablation, and Left Atrial versus Bi-atrial Maze Procedures—

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This study evaluated the efficacy of the left atrial Maze procedure (Lt-maze) and unipolar radiofrequency (RF) ablation as an additional procedure for the surgical treatment of atrial fibrillation (AF) in patient with other cardiac disease.

Methods and Results: The Maze procedure was performed in 100 consecutive patients with AF: Lt-maze, 71 patients; bi-atrial Maze (Bi-maze), 29 patients. Cryoablation and RF ablation were used in 82 and 18 patients, respectively. There were no in-hospital or early deaths. Fourteen patients (14%) experienced postoperative complications. Seventy-five patients (75%) were in sinus rhythm (SR) at discharge, 4 patients were in junctional rhythm, and 21 patients had AF. Two patients (2%) required permanent pacemaker implantation. The AF-free rate at discharge was 79%, and the AF-free rate at hospital discharge did not differ significantly between cryoablation and unipolar RF ablation (78% and 82%, respectively). There were no significant differences between these two groups in operative results, in terms of the aortic cross-clamp time, cardiopulmonary bypass time, and AF-free rate, with the AF-free rate not differing significantly in those who received single valve surgery (73% and 75% in the cryoablation and unipolar RF ablation groups, respectively). The equipment cost of the two procedures differed greatly: 14,000 yen/patient for cryoablation and 250,000 yen/patient for RF ablation. The AF-free rate did not differ significantly between Lt-maze (76%) and Bi-maze (86%), including in those who received single valve surgery (72% and 79%, respectively). The significant predictors of AF recurrence in a univariate analysis were left atrial diameter ($p = 0.03$), duration of AF ($p < 0.01$), fibrillation amplitude on ECG ($p = 0.02$), and cardiothoracic ratio ($p < 0.01$), with the duration of preoperative AF being the only significant predictor of AF in a multivariate analysis.

Conclusion: In this series, unipolar RF ablation for the Maze procedure was as effective as cryoablation at eliminating AF, and Lt-maze and Bi-maze were equipotent at restoring SR at discharge.
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## Introduction

The Maze procedure has been modified several times since it was initially introduced by Cox and colleagues,[1–3] and is now recognized as the standard technique for the treatment of atrial fibrillation (AF). This procedure was originally proposed as a right and left atrial procedure, but its left atrial part (Lt-maze) has received the most attention.[4] The major modification in the history of the Maze procedure has been from the cut-and-sew technique to cryoablation. Nowadays radiofrequency (RF) energy— which is another major modification—is adopted in linear ablation.[5,6] Initially a unipolar RF ablation was introduced clinically, with bipolar RF ablation subsequently being adopted.[7] The Maze procedure has been performed as an additional technique rather than as the main cardiac procedure in our institution. This study evaluated the efficacy of Lt-maze and unipolar RF ablation as additional procedures in the surgical treatment of AF.

## Methods

### Patient selection

From January 1997 through July 2004, 100 consecutive patients underwent surgery for AF using Lt-maze or bi-atrial Maze (Bi-maze), with the modified Cox-Maze III technique being adopted for the latter. The linear blocked lines were ablated with a cryosurgical system (Frigitronics CCS 200, Cooper Surgical, Shelton, CT); from September 2002, a unipolar RF ablation system (COBRA RF System, Boston Scientific, San Jose, CA) was adopted for the Maze procedure. Cryoablation was used for atrial wall isolation in 82 patients, and RF ablation was used in 18 patients; Lt-maze and Bi-maze were performed in 71 and 29 patients, respectively. The primary cardiac disease was valvular disease in 80 patients, ischemic disease in 12 patients, dilated cardiomyopathy in 2 patients, atrial septal defect in 5 patients, and left atrial myxoma in 1 patient.

### Surgical technique

All operations were performed at the same institution by several surgeons. The procedures were performed through a median sternotomy with cardiopulmonary bypass (CPB) and an arrested heart. The left atrium was opened from the right side behind the interatrial groove. In addition to this incision for left atrial entry, linear ablation lesions were created superiorly and posteriorly in order to isolate four pulmonary veins (PVs). The left atrial appendage was either amputated and closed by suture or circumferentially ablated around its base. An ablation line was created from the base of this appendage to the PVs island, and from the mitral annulus to the PVs island. An inferior isthmus ablation was performed in the right atrium (RA). In the case of Bi-maze, an L-shaped incision was made on the right atrial lateral wall laterally and posteriorly. A linear ablation lesion was created from the posterior edge of this RA entry to the inferior vena cava (IVC), and from the anterior end of this RA incision to the tricuspid valve annulus. The right atrial appendage was amputated and closed by
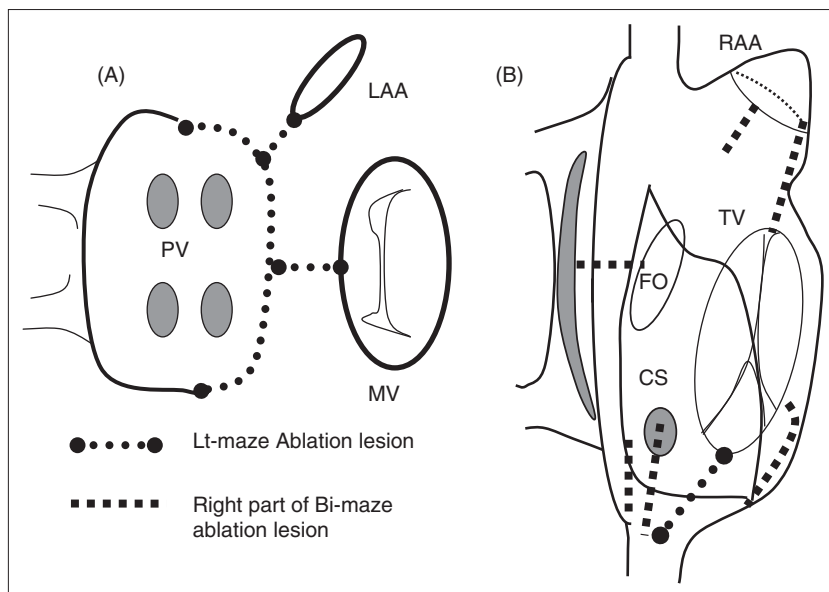


**Figure 1**  Schematic drawings of the Maze procedures.
(A) left atrial part of the Maze procedure, (B) right atrial part of the Maze procedure
PV: pulmonary vein, MV: mitral valve, LAA: left atrial appendage, CS: coronary sinus, TV: tricuspid valve, FO: fossa ovalis, RAA: right atrial appendage

suture. An ablation line was created from the base of the appendage to the tricuspid valve annulus. In case of extremely dilated RA, another ablation line was added on the RA free wall from the base of the appendage. The additional linear ablation lesion was created between the coronary sinus (CS) and IVC in order to eliminate the atrial tachycardia originating from CS and also reinforce the incomplete ablation lesion of the RA entry–IVC around the cannulated IVC.[8–11] The atrial septum was ablated from both atrial primary incisions to the fossa ovalis (**Figure 1**). The cryoablation and RF ablation were performed at $-60°C$ for 90 seconds and $80°C$ for 60 seconds, respectively.

### Data analysis

All analyses were performed retrospectively using StatView software (ver. 5.0, SAS Institute, Cary, NC). Continuous data are expressed as mean $\pm$ standard deviation values unless otherwise specified. Differences in categorized variables were tested by $\chi^2$ tests, and those in continuous variables were tested by $t$ tests or the Mann-Whitney $U$ test. The ablation technique and the Maze procedure were compared separately in this study: for the ablation comparison, the study cohort was divided into cryoablation (Cryo) and RF-ablation (RF) groups; and for the Maze procedure, the cohort was divided into Bi-maze and Lt-maze groups. Furthermore, these comparative analyses were performed in patient subgroups that underwent a single valve procedure including valvuloplasty or mitral or aortic valve replacement with or without tricuspid valve

annuloplasty. Logistic regression analysis was used to estimate the predictor of AF recurrence. First the association between AF recurrence and each of the other possible predictors was quantified by univariate analysis, and then all predictors for which $p < 0.10$ in the univariate analysis were included in the multivariate logistic regression model except tricuspid valve annuloplasty (TAP). P value of other factors for which $p > 0.10$ in univariate analysis was rather high, while TAP $(p = 0.13)$ was the only factor in which the p value was fairly close to 0.10 and age was a generally related factor of AF. A probability value of $p \leq 0.05$ was considered indicative of statistical significance.

### Results

There were no in-hospital or early deaths. Fourteen patients (14%) experienced postoperative complications: transient stroke in 3 patients, low output syndrome in 9 patients, and embolism in 2 patients (one was ischemic colitis and ischemic angiopathy in the lower extremities with AF, the other was embolism in the central artery of the retina in SR). Seventy-five patients (75%) were in sinus rhythm (SR) at discharge, 4 patients were in junctional rhythm, and 21 patients had AF. Two patients (2%) required permanent pacemaker implantation before discharge. The AF-free rate at discharge was 79%.

### Comparison 1: Ablation device—cryoablation vs. unipolar RF ablation

The clinical characteristics of patients in the Cryo and RF groups are listed in **Table 1**, for which the only significant difference was in gender: the proportion of males was significantly higher in the RF group than in the Cryo group. The AF-free rates at hospital discharge were 78.1% and 82.4% in the Cryo and RF groups, respectively. There were no significant differences between the two groups in operative results, in terms of the aortic cross-clamp

**Table 1** Patients' characteristics in ablation-device comparison groups.

|  | Cryoablation:<br>n = 82<br>(single valve:<br>n = 52) | RF ablation:<br>n = 18<br>(single valve:<br>n = 8) |  |
|---|---|---|---|
| Age, years | 59.8 ± 9.3 | 60.3 ± 11.6 | N.S. |
|  | (57.9 ± 10.0) | (58.5 ± 11.5) | N.S. |
| Gender, M/F | 40/42 | 16/2 | p < 0.01 |
|  | (24/28) | (8/0) | p = 0.013 |
| AF duration,<br>years | 6.3 ± 5.7 | 7.1 ± 7.9 | N.S. |
|  | (6.7 ± 5.9) | (8.9 ± 8.7) | N.S. |
| Fibrillation<br>amplitude, mV | 0.20 ± 0.09 | 0.21 ± 0.08 | N.S. |
|  | (0.19 ± 0.09) | (0.21 ± 0.10) | N.S. |
| LAD, mm | 49.1 ± 9.1 | 50.3 ± 7.2 | N.S. |
|  | (50.5 ± 9.6) | (53.0 ± 5.5) | N.S. |

( ): subgroup with single valve surgery, N.S.: no significant, LAD: left atrial diameter

**Table 2** Operative results in ablation comparison.

|  | Cryoablation | RF ablation |  |
|---|---|---|---|
| ACC time, min | 133.1 ± 37.0 | 119.1 ± 33.9 | N.S. |
|  | (121.8 ± 25.8) | (113.0 ± 30.0) | (N.S.) |
| CPB time, min | 189.1 ± 47.0 | 180.6 ± 48.7 | N.S. |
|  | (175.9 ± 38.8) | (170.8 ± 56.6) | (N.S.) |
| Defibrillation rate, % | 78.1 | 82.4 | N.S. |
|  | (73.1) | (75.0) | (N.S.) |

( ): subgroup with single valve surgery, ACC: aortic cross-clamp, CPB: cardiopulmonary bypass

(ACC) time, CPB time, and AF-free rate. In those who received single valve surgery, the AF-free rates at hospital discharge were 73.1% and 75.0% in the Cryo and RF groups, respectively, and there was no significant difference between these groups in ACC time, CPB time, or AF-free rate (**Table 2**).

### Comparison 2: Maze procedure—Lt-maze vs. Bi-maze

The clinical characteristics of patients in the Lt-maze and Bi-maze groups are listed in **Table 3**, for which there were no significant differences. The AF-free rates at hospital discharge were 76.1% and 86.2% in the Lt-maze and Bi-maze groups, respectively, and there was no significant difference between these groups in ACC time, CPB time, and AF-free rate. In those who received single valve surgery, the AF rates at hospital discharge were 71.7% and 78.6% in the Lt-maze and Bi-maze groups, respectively, and there was no significant difference between these groups in ACC time, CPB time, and AF-free rate (**Table 4**).

**Table 3** Patients' characteristics in Maze-procedure comparison groups.

| | Lt-maze: n = 71 (single valve: n = 46) | Bi-maze: n = 29 (single valve: n = 14) | |
|---|---|---|---|
| Age, years | 60.3 ± 10.0 | 58.7 ± 9.1 | N.S. |
| | (58.1 ± 10.4) | (57.7 ± 9.3) | (N.S.) |
| Gender, M/F | 36/35 | 20/9 | N.S. |
| | (21/25) | (11/3) | (p = 0.03) |
| AF duration, years | 6.7 ± 6.2 | 5.8 ± 6.0 | N.S. |
| | (6.9 ± 6.1) | (7.5 ± 7.2) | (N.S.) |
| Fibrillation amplitude, mV | 0.19 ± 0.09 | 0.23 ± 0.09 | N.S. |
| | (0.19 ± 0.08) | (0.21 ± 0.11) | (N.S.) |
| LAD, mm | 49.4 ± 8.7 | 49.1 ± 9.1 | N.S. |
| | (50.7 ± 9.5) | (51.4 ± 8.1) | (N.S.) |

(   ): subgroup with single valve surgery

### AF predictor

A univariate analysis identified the preoperative left atrial diameter (p = 0.03), duration of preoperative AF (p < 0.01), preoperative fibrillation amplitude on ECG (p = 0.02), and preoperative cardiothoracic ratio (p < 0.01) as the significant predictors of AF at discharge. Duration of preoperative AF was the only significant predictor of AF at discharge in multivariate analysis (**Table 5**). The perioperative variables of ablation device, Maze procedure, ACC time, and CPB time were not found to be significant predictors of AF at discharge.

### Cost

For cryoablation, the initial cost including the probes and operating console is approximately 7.3 million yen, and the running cost of the required nitrous oxide gas is less than 14,000 yen/patient. For unipolar RF ablation, the initial cost of the operating console is approximately 2.1 million yen, and running cost of the disposable probes is approximately 250,000 yen/patient.

### Discussion

Since the Maze procedure was introduced and modified by Cox and colleagues, this unique technique has become widespread as a surgical treatment

**Table 4** Operative results in Maze-procedure comparison.

| | Lt-maze | Bi-maze | |
|---|---|---|---|
| ACC time, min | 129.3 ± 34.2 | 131.8 ± 41.7 | N.S. |
| | (121.9 ± 25.4) | (116.6 ± 29.7) | (N.S.) |
| CPB time, min | 187.0 ± 48.6 | 187.5 ± 44.6 | N.S. |
| | (174.2 ± 39.7) | (178.9 ± 46.7) | (N.S.) |
| Defibrillation rate, % | 76.1 | 86.2 | N.S. |
| | (71.7) | (78.6) | (N.S.) |

(   ): subgroup with single valve surgery

**Table 5** Predictor of postoperative AF.

| | Univariate | Multivariate | | |
|---|---|---|---|---|
| | p | p | Hazard ratio | 95% Confidential interval |
| Age | 0.3239 | 0.865 | 0.992 | 0.908–1.084 |
| Tricuspid annuloplasty | 0.129 | 0.538 | 0.614 | 0.130–2.905 |
| LAD | 0.0289 | 0.283 | 0.952 | 0.870–1.042 |
| Cardiothoracic ratio | 0.0157 | 0.452 | 0.954 | 0.844–1.078 |
| Duration of AF | 0.0001 | 0.019 | 0.869 | 0.773–0.977 |
| Fibrillation amplitude | 0.0113 | 0.109 | 1579 | 0.193–12964 |

for AF. Several modified procedures have been performed and reported by several surgeons, such as Kosakai and associates,[12] Sueda and associates,[4] and Isobe and associates.[13] However, the decision to use Maze as the main procedure or additional procedures varies between surgeons and institutions, with this influencing not only the strategy and concept of treatment for AF but also the results of SR restoration. Furthermore, the results can be influenced by the indication for the Maze procedure, and hence the SR restoration rate after surgery would be improved if the indication was accurately limited. Our contra-indication was only a low amplitude of the fibrillation wave in electrocardiogram, because postoperative persistent bradycardia, which sometimes resulted in permanent pacemaker implantation, should be avoided; the fine fibrillation wave is associated with atrial fibrosis and more non-uniform atrial excitement, namely electrical remodeling.[14,15] The maintenance of regular cardiac rhythm helps to decrease the risk of thromboembolism and improve cardiac function. Even if SR is maintained for only several weeks after surgery, this provides the advantage of stable hemodynamic management in the postoperative recovery period.[16] Therefore, we have performed the Maze procedure as an additional technique with wide indications.

In several published reports the SR restoration rate ranges from 79% to 95%, and the mortality ranges from 0% to 6.8%.[17–20] We therefore consider our SR restoration and mortality rates of 79% and 0%, respectively, to be satisfactory.

The left atrial part of the Maze procedure was focused on, and performed as the so-called Lt-maze. The efficacy of Lt-maze has already been reported on by Sueda and colleagues. For patients with only a right atrial focus, Lt-maze may bring little effect. However, most patients with AF can benefit from Lt-maze, since some studies have demonstrated that the most common focus of AF is in the left atrium, especially the area around the PVs.[21,22] We select Lt-maze except in cases with severe tricuspid valve regurgitation. Since increased volume and/or filling pressure in RA induced by tricuspid valve regurgitation and atrial septal defect bring on the thinning and fibrosis of myocardium and conducting fibers which lead to AF, we perform the Bi-maze procedure.[23–25] Although there are some reports of Lt-maze reducing the ACC and CPB times, we found no statistically significant differences in these variables between Lt-maze and Bi-maze. The reason for this is that some ablation lesions of the right part of Bi-maze could be created after aortic unclamp during CPB weaning.

Predictors of persistent preoperative AF have been reported by several investigators. In this study, univariate logistic regression analysis showed that a large left atrium, long duration of AF, low fibrillation amplitude at V1 on ECG, and high cardiothoracic ratio are significant predictors at discharge; however, the multivariate logistic regression analysis showed that long duration of AF is a significant predictor. The long-term presence of AF (i.e., over a period of years) causing atrial stretch results in decreases in muscle volume and fibrotic changes in atria.[23,26,27] AF can lead to an altered patterns of connexins, changes in myocyte cellular substructure, interstitial fibrosis, and apoptotic atrial myocyte death.[28] Sinus node disease also shows similar observations and low atrial voltage causing pathophysiological change.[29] Degeneration and/or fibrosis of atrium including sinus node and conducting fiber cause tissue inhomogeneity and nonuniform atrial excitement. Fibroblast which is fairly depolarized influences adjacent cell depolarization by an electrotonic interaction. The degree of these atrial changes reflects on the fibrillation amplitude and plays a role in the recurrence of AF and sinus node disease after surgery.[14,15,30–33] In order to reduce complications, we carefully consider not only the AF duration but also the fibrillation amplitude for contraindications in order to avoid postoperative persistent bradycardia. In other words, a high fibrillation amplitude despite a long AF duration is judged as an indication.

The flexible probe of the unipolar RF ablation system (which integrates multiple electrodes) can fit into the curved surface of the atrium and be used to make a long ablation line. We expected that the RF ablation system would result in short ACC and CPB times. However, the absence of significant differences in these variables between cryoablation and RF ablation in our study may be attributable to the use of two cryoprobes simultaneously for the Maze procedure with cryoablation.

It is important to note new risks associated with unipolar RF ablation. Gillinov and colleagues,[34] and Mohr and colleagues[35] reported esophageal injuries associated with unipolar RF ablation, and microembolization and hemostatic activation in percutaneous RF catheter ablation were reported by Anfinsen and colleagues,[36] and Kok and colleagues.[37] Since it is possible that such complications occur in the Maze procedure, we minimize the blood around the RF probe and routinely irrigate the left atrium with saline solution after RF ablation in order to wash out char.

The financial aspects of medical treatments also

need to be considered. The initial cost of the cryoablation system is more expensive than that of the RF ablation system, however the running cost of the RF ablation system is much higher than that of the cryoablation system. According to simple accounting of material cost in the RF ablation, the advantage of the initial cost was offset by the high running cost of only 22 cases. Therefore it seems reasonable to suppose that the cryoablation system contributes to cost reduction. Japanese medical insurance does not yet cover the expensive disposable RF ablation probe. Although RF ablation is as effective as cryoablation, this RF ablation system may not be economically appropriate in Japan—a demonstration of the overwhelming superiority of RF ablation may be necessary to obtain approval for medical insurance coverage. Therefore, the RF ablation probe is used for limited indications, such as beating heart surgery, in our institution.

Regarding SR restoration rate in this series in which all Maze procedures were performed with arrested heart, there was no significant difference between RF ablation and cryoablation. However the strategy of AF treatment will be changed by the use of RF ablation, since it enables the Maze procedure in the beating heart to be performed with an epicardial approach; in contrast, it is impossible to make a complete ablation lesion with cryoablation. Additionally since it is possible to pace and measure over the ablation line in the beating heart, this procedure enable to confirm the presence of atrial wall conduction, and determine whether or not the ablated block line is completed; this improves the success rate of the Maze procedure.

### Study limitations

This study was a retrospective analysis of a rather small number of patients in the early postoperative period, and hence the conclusions therefrom should be limited to this period. Mid- and long-term data should be analyzed and further follow-up is required to evaluate the long-term efficacy of the various procedures.

## Conclusion

Unipolar RF ablation for the Maze procedure is as effective as cryoablation at eliminating AF. However, the cost of the RF ablation probe needs to be reduced. The Lt-maze and Bi-maze procedures are equipotent at restoring SR at discharge, and the preoperative duration of AF was the only detected significant predictor of AF recurrence.

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