

Cardiac magnetic resonance in clinical cardiology

Andreas Kumar, Rodrigo Bagur

Andreas Kumar, Rodrigo Bagur, Division of Cardiology, Department of Medicine, Quebec University Hospital Centre, G1R 2J6 Quebec, Canada

Author contributions: Both authors contributed to this manuscript.

Conflict-of-interest: The authors report no conflicts of interest regarding the content herein.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Rodrigo Bagur, MD, PhD, FAHA, Attending Cardiologist and Interventional Cardiologist, Division of Cardiology, Department of Medicine, Quebec University Hospital Centre, 11 Côte du Palais, L'Hôtel-Dieu de Québec, G1R 2J6 Quebec, Canada. rodrigobagur@yahoo.com

Telephone: +1-418-6915022

Fax: +1-418-6915714

Received: October 27, 2014

Peer-review started: October 28, 2014

First decision: November 27, 2014

Revised: December 9, 2014

Accepted: December 29, 2014

Article in press: January 4, 2015

Published online: January 26, 2015

Abstract

Over the last decades, cardiac magnetic resonance (CMR) has transformed from a research tool to a widely used diagnostic method in clinical cardiology. This method can now make useful, unique contributions to the work-up of patients with ischemic and non-ischemic heart disease. Advantages of CMR, compared to other imaging methods, include very high resolution imaging with a spatial resolution up to 0.5 mm × 0.5 mm in plane, a large array of different imaging sequences to provide *in vivo* tissue characterization, and radiation-free imaging. The present manuscript highlights the

relevance of CMR in the current clinical practice and new perspectives in cardiology.

Key words: Cardiac magnetic resonance; Gadolinium enhancement; Myocarditis; Myocardial; Cardiomyopathy

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The present manuscript highlights the relevance of cardiac magnetic resonance in the current clinical practice and new perspectives in cardiology.

Kumar A, Bagur R. Cardiac magnetic resonance in clinical cardiology. *World J Cardiol* 2015; 7(1): 6-9 Available from: URL: <http://www.wjgnet.com/1949-8462/full/v7/i1/6.htm> DOI: <http://dx.doi.org/10.4330/wjc.v7.i1.6>

INTRODUCTION

Over the last decades, cardiac magnetic resonance (CMR) has transformed from a research tool to a widely used diagnostic method in clinical practice. While other imaging modalities like echocardiography and cardiac computed tomography depend solely on tissue density, the most important feature that CMR affords to the diagnostic toolset of the clinic cardiologist, is its ability to provide with a very-high spatial resolution, up to 0.5 mm × 0.5 mm in plane, a large array of different imaging sequences in order to assess *in-vivo* tissue characterization, in addition to radiation-free imaging. These imaging sequences investigate the presence of protons in different chemical environments, thereby allowing conclusions on the presence of fat, water (edema), blood or myocardium among other tissues. The addition of a contrast agent enhances the diagnostic capabilities to assess perfusion, fibrosis and necrosis as well as identify thrombus. Exploiting these different imaging sequences, in addition to the capability of performing high spatial resolution imaging in any desired imaging plane in 3-dimension (3D)

space, CMR provides what could be also called “*in-vivo* pathology”. Therefore, this has led to substantial progress in the assessment of patients with ischemic and non-ischemic heart disease^[1].

ISCHEMIC HEART DISEASE

Acute ischemic disease

After the development of electrocardiographic-triggered fast CMR imaging using gradient-echo sequences, the late gadolinium enhancement (LGE) imaging technique opened new horizons for CMR at the beginning of the century^[2-4]. The method exploits the fact that gadolinium-based contrast agents have a much higher volume of distribution in necrotic and fibrotic tissue, when the cardiomyocytes have lost their cell wall integrity or have been replaced by collagen. Late enhancement imaging therefore allows for an assessment of viability with unprecedented image contrast and very-high spatial resolution. Clinical applications included the detection, when the diagnosis is unclear, the differences between acute myocardial infarction (AMI) and chronic ischemic cardiomyopathy^[5,6]. The assessment of viability predicts functional recovery in acute myocardial infarction based on the transmural extent of the necrosis^[7].

The use of CMR in this setting was subsequently enhanced by the development of water-sensitive T2-STIR sequences, allows the assessment of tissue edema. Of note, since only acute infarction has edema, the combination with LGE imaging, T2-STIR helps to differentiate acute from chronic myocardial infarction^[6,8,9]. The edematous tissue in AMI is thought to reflect the area-at-risk, allowing for quantitative assessment of salvaged myocardium after reperfusion therapy^[10-12]. This can be measured as the difference between edematous tissue minus necrotic tissue, where the latter is seen on LGE.

Microvascular obstruction (MVO) as a consequence of ischemia and reperfusion injury in AMI is reliably detected with first-pass perfusion imaging or the LGE sequence applied early after contrast injection. The presence of MVO is an independent predictor of adverse outcome, independent of infarct size and left ventricular systolic function^[13,14]. Severe microvascular injury can be complicated by reperfusion hemorrhage, which again can be visualized and also quantified with a specific CMR sequence (T2*-weighted imaging)^[15]. It is currently unclear whether hemorrhage has independent prognostic effects beyond MVO, since insufficient sample size and flaws in study design, limited most of the clinical studies trying to address this question.

Chronic ischemic disease

Newer imaging approaches are emerging to fine-tune risk assessment in chronic ischemic heart disease, and help, for example, with patient's selection for implantable cardioverter-defibrillators (ICD) implantation. Several authors have shown that the peri-infarct zone between

chronic infarction tissue and healthy myocardium displays an intermediate contrast signal. The extent of this “grey-zone” has been associated with ventricular arrhythmia and major adverse cardiac events, probably due to electrical re-entry circuits being located in this area^[16]. Prospective studies are under way to assess, whether advanced tissue characteristics such as the LGE grey-zone would be helpful to better select patients for ICD implantation, thereby switching selection criteria from the current left ventricular systolic function to a tissue characteristic. Hence, an improved patient's selection could be of tremendous help, allowing for better selection of patients at higher risk, and also avoiding potentially unnecessary ICD implantations.

In stable coronary artery disease, CMR perfusion imaging with and without stress agents (predominantly adenosine) can detect myocardial ischemia with high accuracy. Depending on the reference standard, it has been reported a sensitivity and specificity of about 90% and 70%-90%, respectively, for the detection of myocardial ischemia^[17,18]. Advantages of CMR in this setting include a higher spatial resolution than nuclear imaging methods, allowing the diagnosis of sub-endocardial perfusion defects and microvascular disease^[19]. Research efforts are under way to detect ischemia without using contrast agents. Indeed, blood-oxygen-level-dependent (BOLD) sequences are able to create image contrast-based on the tissue's oxygen content in the brain, and initial reports have suggested that modified BOLD sequences could also be applied in the heart^[20,21]. This approach, once developed to a clinically applicable tool, promises to revolutionize the ischemia detection field by measuring myocardial oxygen directly, and moving away from perfusion as a surrogate marker.

NON-ISCHEMIC HEART DISEASE

Cardiac magnetic resonance has allowed significant progress in understanding of non-ischemic cardiomyopathies. Beyond accurate assessment of ventricular volume and function, tissue characterization using T1, T2, T2*, perfusion and contrast-enhanced sequences allows for comprehensive tissue characterization as a non-invasive pathology^[22-24]. This further contributes to identify the etiology of heart failure, and initial studies have started to identify CMR-based tissue characteristics as prognostic markers^[25-28]. In fact, CMR is now the reference diagnostic tool to diagnose myocarditis, as recommended by the Lake Louise consensus criteria^[29]. Importantly, T2-weighted imaging identifies edema as a marker of inflammation in acute/active disease, and late gadolinium enhancement is typically present in a “patchy”, thus, a non-ischemic pattern. Of note, the combined imaging sequences yield a diagnostic power to assess myocarditis with a sensitivity of 76% and specificity of 96%^[30]. Noteworthy, patients with LGE in myocarditis have a worse prognosis than patients

without LGE^[31]. Moreover, infiltrative cardiomyopathies such as amyloidosis are reliably diagnosed based on their typical pattern of signal change on T2 and LGE, usually involving the entire myocardium as an organ^[32]. The diagnostic power of CMR is especially well exploited in iron deposition disease like thalassemia and hemochromatosis. In fact, CMR can semi-quantitatively assess iron deposition by measuring the T2* value of myocardium. The latter highly correlates with myocardial iron content^[33,34]. Furthermore, it is of prognostic value as can be used to monitor the effect of iron chelation therapy, let's say, to start, titrate or finish iron chelation therapy.

THE FUTURE OF CMR

Cardiac magnetic resonance is still a relatively “young” imaging technique, and new technical developments are continuously entering the clinical arena. While current imaging sequences mostly provide a contrast suited for visual analysis, imaging methods that quantitatively map T1, T2 and T2* characteristics are under evaluation^[35]. Moving away from qualitative assessment to semi-quantitative or quantitative image analysis will allow increased diagnostic accuracy and reduced observer bias, as well as improve inter-study variability. Normal values will have to be established for different field strengths, and differences in sequence programming between different CMR vendors as a source of variability of normal values will have to be addressed. Eventually, advanced tissue characterization with mapping sequences could reduce (but probably not eliminate) the dependence on gadolinium-based contrast agent. New imaging sequences that apply self-triggering may eliminate the need for electrocardiographic tracing and breath-hold maneuvers^[36], further increasing patient comfort and reduce scan time.

CONCLUSION

Cardiac magnetic resonance has become a basic diagnostic tool in cardiovascular medicine. The next decade will be marked by clinical trials investigating the prognostic value of the detailed imaging findings that can be obtained today, and may guide therapy and improve patient prognosis.

REFERENCES

- 1 **Kumar A**, Patton DJ, Friedrich MG. The emerging clinical role of cardiovascular magnetic resonance imaging. *Can J Cardiol* 2010; **26**: 313-322 [PMID: 20548977]
- 2 **Simonetti OP**, Kim RJ, Fieno DS, Hillenbrand HB, Wu E, Bundy JM, Finn JP, Judd RM. An improved MR imaging technique for the visualization of myocardial infarction. *Radiology* 2001; **218**: 215-223 [PMID: 11152805]
- 3 **Kim RJ**, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 1999; **100**: 1992-2002 [PMID: 10556226]
- 4 **Kim RJ**, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O, Klocke FJ, Bonow RO, Judd RM. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med* 2000; **343**: 1445-1453 [PMID: 11078769]
- 5 **Kwong RY**, Schussheim AE, Rekhraj S, Aletras AH, Geller N, Davis J, Christian TF, Balaban RS, Arai AE. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. *Circulation* 2003; **107**: 531-537 [PMID: 12566362]
- 6 **Cury RC**, Shash K, Nagurney JT, Rosito G, Shapiro MD, Nomura CH, Abbara S, Bamberg F, Ferencik M, Schmidt EJ, Brown DF, Hoffmann U, Brady TJ. Cardiac magnetic resonance with T2-weighted imaging improves detection of patients with acute coronary syndrome in the emergency department. *Circulation* 2008; **118**: 837-844 [PMID: 18678772]
- 7 **Gerber BL**, Garot J, Bluemke DA, Wu KC, Lima JA. Accuracy of contrast-enhanced magnetic resonance imaging in predicting improvement of regional myocardial function in patients after acute myocardial infarction. *Circulation* 2002; **106**: 1083-1089 [PMID: 12196333]
- 8 **Abdel-Aty H**, Zagrosek A, Schulz-Menger J, Taylor AJ, Messroghli D, Kumar A, Gross M, Dietz R, Friedrich MG. Delayed enhancement and T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. *Circulation* 2004; **109**: 2411-2416 [PMID: 15123531]
- 9 **Abdel-Aty H**, Cocker M, Meek C, Tyberg JV, Friedrich MG. Edema as a very early marker for acute myocardial ischemia: a cardiovascular magnetic resonance study. *J Am Coll Cardiol* 2009; **53**: 1194-1201 [PMID: 19341860]
- 10 **Aletras AH**, Tilak GS, Natanzon A, Hsu LY, Gonzalez FM, Hoyt RF, Arai AE. Retrospective determination of the area at risk for reperfused acute myocardial infarction with T2-weighted cardiac magnetic resonance imaging: histopathological and displacement encoding with stimulated echoes (DENSE) functional validations. *Circulation* 2006; **113**: 1865-1870 [PMID: 16606793]
- 11 **Raman SV**, Simonetti OP, Winner MW, Dickerson JA, He X, Mazzaferri EL, Ambrosio G. Cardiac magnetic resonance with edema imaging identifies myocardium at risk and predicts worse outcome in patients with non-ST-segment elevation acute coronary syndrome. *J Am Coll Cardiol* 2010; **55**: 2480-2488 [PMID: 20510215]
- 12 **Larose E**, Tizon-Marcos H, Rodés-Cabau J, Rinfret S, Déry JP, Nguyen CM, Gleeton O, Boudreault JR, Roy L, Noël B, Proulx G, Rouleau J, Barbeau G, De Larocheillère R, Bertrand OF. Improving myocardial salvage in late presentation acute ST-elevation myocardial infarction with preproliferation embolic protection. *Catheter Cardiovasc Interv* 2010; **76**: 461-470 [PMID: 20506154]
- 13 **Nijveldt R**, Hofman MB, Hirsch A, Beek AM, Umans VA, Algra PR, Piek JJ, van Rossum AC. Assessment of microvascular obstruction and prediction of short-term remodeling after acute myocardial infarction: cardiac MR imaging study. *Radiology* 2009; **250**: 363-370 [PMID: 19164698]
- 14 **Hamirani YS**, Wong A, Kramer CM, Salerno M. Effect of microvascular obstruction and intramyocardial hemorrhage by CMR on LV remodeling and outcomes after myocardial infarction: a systematic review and meta-analysis. *JACC Cardiovasc Imaging* 2014; **7**: 940-952 [PMID: 25212800]
- 15 **Kumar A**, Green JD, Sykes JM, Ephrat P, Carson JJ, Mitchell AJ, Wisenberg G, Friedrich MG. Detection and quantification of myocardial reperfusion hemorrhage using T2*-weighted CMR. *JACC Cardiovasc Imaging* 2011; **4**: 1274-1283 [PMID: 22172784 DOI: 10.1016/j.jcmg.2011.08.016]
- 16 **Yan AT**, Shayne AJ, Brown KA, Gupta SN, Chan CW, Luu TM, Di Carli MF, Reynolds HG, Stevenson WG, Kwong RY. Characterization of the peri-infarct zone by contrast-

- enhanced cardiac magnetic resonance imaging is a powerful predictor of post-myocardial infarction mortality. *Circulation* 2006; **114**: 32-39 [PMID: 16801462]
- 17 **Schwitzer J**, Wacker CM, van Rossum AC, Lombardi M, Al-Saadi N, Ahlstrom H, Dill T, Larsson HB, Flamm SD, Marquardt M, Johansson L. MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial. *Eur Heart J* 2008; **29**: 480-489 [PMID: 18208849 DOI: 10.1093/eurheartj/ehm617]
 - 18 **Schwitzer J**, Wacker CM, Wilke N, Al-Saadi N, Sauer E, Huettle K, Schönberg SO, Luchner A, Strohm O, Ahlstrom H, Dill T, Hoebel N, Simor T. MR-IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary artery disease Trial: perfusion-cardiac magnetic resonance vs. single-photon emission computed tomography for the detection of coronary artery disease: a comparative multicentre, multivendor trial. *Eur Heart J* 2013; **34**: 775-781 [PMID: 22390914 DOI: 10.1093/eurheartj/ehs022]
 - 19 **Panting JR**, Gatehouse PD, Yang GZ, Grothues F, Firmin DN, Collins P, Pennell DJ. Abnormal subendocardial perfusion in cardiac syndrome X detected by cardiovascular magnetic resonance imaging. *N Engl J Med* 2002; **346**: 1948-1953 [PMID: 12075055]
 - 20 **Karamitsos TD**, Leccisotti L, Arnold JR, Recio-Mayoral A, Bhamra-Ariza P, Howells RK, Searle N, Robson MD, Rimoldi OE, Camici PG, Neubauer S, Selvanayagam JB. Relationship between regional myocardial oxygenation and perfusion in patients with coronary artery disease: insights from cardiovascular magnetic resonance and positron emission tomography. *Circ Cardiovasc Imaging* 2010; **3**: 32-40 [PMID: 19920032 DOI: 10.1161/CIRCIMAGING.109.860148]
 - 21 **Friedrich MG**, Niendorf T, Schulz-Menger J, Gross CM, Dietz R. Blood oxygen level-dependent magnetic resonance imaging in patients with stress-induced angina. *Circulation* 2003; **108**: 2219-2223 [PMID: 14557359]
 - 22 **Treibel TA**, White SK, Moon JC. Myocardial Tissue Characterization: Histological and Pathophysiological Correlation. *Curr Cardiovasc Imaging Rep* 2014; **7**: 9254 [PMID: 25258658]
 - 23 **Satoh H**, Sano M, Suwa K, Saitoh T, Nobuhara M, Saotome M, Urushida T, Katoh H, Hayashi H. Distribution of late gadolinium enhancement in various types of cardiomyopathies: Significance in differential diagnosis, clinical features and prognosis. *World J Cardiol* 2014; **6**: 585-601 [PMID: 25068019 DOI: 10.4330/wjc.v6.i7.585]
 - 24 **Gottlieb I**, Macedo R, Bluemke DA, Lima JA. Magnetic resonance imaging in the evaluation of non-ischemic cardiomyopathies: current applications and future perspectives. *Heart Fail Rev* 2006; **11**: 313-323 [PMID: 17131077]
 - 25 **Perazzolo Marra M**, De Lazzari M, Zorzi A, Migliore F, Zilio F, Calore C, Vettor G, Tona F, Tarantini G, Cacciavillani L, Corbetti F, Giorgi B, Miotto D, Thiene G, Basso C, Iliceto S, Corrado D. Impact of the presence and amount of myocardial fibrosis by cardiac magnetic resonance on arrhythmic outcome and sudden cardiac death in nonischemic dilated cardiomyopathy. *Heart Rhythm* 2014; **11**: 856-863 [PMID: 24440822 DOI: 10.1016/j.hrthm.2014.01.014]
 - 26 **Almeahadi F**, Joncas SX, Nevis I, Zahrani M, Bokhari M, Stirrat J, Fine NM, Yee R, White JA. Prevalence of myocardial fibrosis patterns in patients with systolic dysfunction: prognostic significance for the prediction of sudden cardiac arrest or appropriate implantable cardiac defibrillator therapy. *Circ Cardiovasc Imaging* 2014; **7**: 593-600 [PMID: 24902587 DOI: 10.1161/CIRCIMAGING.113.001768]
 - 27 **Barone-Rochette G**, Piérard S, De Meester de Ravenstein C, Seldrum S, Melchior J, Maes F, Pouleur AC, Vancraeynest D, Pasquet A, Vanoverschelde JL, Gerber BL. Prognostic significance of LGE by CMR in aortic stenosis patients undergoing valve replacement. *J Am Coll Cardiol* 2014; **64**: 144-154 [PMID: 25011718 DOI: 10.1016/j.jacc.2014.02.612]
 - 28 **Chan RH**, Maron BJ, Olivetto I, Pencina MJ, Assenza GE, Haas T, Lesser JR, Gruner C, Crean AM, Rakowski H, Udelson JE, Rowin E, Lombardi M, Cecchi F, Tomberli B, Spirito P, Formisano F, Biagini E, Rapezzi C, De Cecco CN, Autore C, Cook EF, Hong SN, Gibson CM, Manning WJ, Appelbaum E, Maron MS. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation* 2014; **130**: 484-495 [PMID: 25092278 DOI: 10.1161/CIRCULATIONAHA.113.007094]
 - 29 **Friedrich MG**, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, White JA, Abdel-Aty H, Gutberlet M, Prasad S, Aletas A, Laissy JP, Paterson I, Filipchuk NG, Kumar A, Pauschinger M, Liu P. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper. *J Am Coll Cardiol* 2009; **53**: 1475-1487 [PMID: 19389557 DOI: 10.1016/j.jacc.2009.02.007]
 - 30 **Abdel-Aty H**, Boyé P, Zagrosek A, Wassmuth R, Kumar A, Messroghli D, Bock P, Dietz R, Friedrich MG, Schulz-Menger J. Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. *J Am Coll Cardiol* 2005; **45**: 1815-1822 [PMID: 15936612]
 - 31 **Grün S**, Schumm J, Greulich S, Wagner A, Schneider S, Bruder O, Kispert EM, Hill S, Ong P, Klingel K, Kandolf R, Sechtem U, Mahrholdt H. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. *J Am Coll Cardiol* 2012; **59**: 1604-1615 [PMID: 22365425 DOI: 10.1016/j.jacc.2012.01.007]
 - 32 **Syed IS**, Glockner JF, Feng D, Araoz PA, Martinez MW, Edwards WD, Gertz MA, Dispenzieri A, Oh JK, Bellavia D, Tajik AJ, Grogan M. Role of cardiac magnetic resonance imaging in the detection of cardiac amyloidosis. *JACC Cardiovasc Imaging* 2010; **3**: 155-164 [PMID: 20159642 DOI: 10.1016/j.jcmg.2009.09.023]
 - 33 **Carpenter JP**, Grasso AE, Porter JB, Shah F, Dooley J, Pennell DJ. On myocardial siderosis and left ventricular dysfunction in hemochromatosis. *J Cardiovasc Magn Reson* 2013; **15**: 24 [PMID: 23509881 DOI: 10.1186/1532-429X-15-24]
 - 34 **Pennell DJ**, Udelson JE, Arai AE, Bozkurt B, Cohen AR, Galanello R, Hoffman TM, Kiernan MS, Lerakis S, Piga A, Porter JB, Walker JM, Wood J. Cardiovascular function and treatment in β -thalassemia major: a consensus statement from the American Heart Association. *Circulation* 2013; **128**: 281-308 [PMID: 23775258 DOI: 10.1161/CIR.0b013e31829b2be6]
 - 35 **Moon JC**, Messroghli DR, Kellman P, Piechnik SK, Robson MD, Ugander M, Gatehouse PD, Arai AE, Friedrich MG, Neubauer S, Schulz-Menger J, Schelbert EB. Myocardial T1 mapping and extracellular volume quantification: a Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement. *J Cardiovasc Magn Reson* 2013; **15**: 92 [PMID: 24124732 DOI: 10.1186/1532-429X-15-92]
 - 36 **Sharif B**, Dharmakumar R, Arsanjani R, Thomson L, Bairey Merz CN, Berman DS, Li D. Non-ECG-gated myocardial perfusion MRI using continuous magnetization-driven radial sampling. *Magn Reson Med* 2014; **72**: 1620-1628 [PMID: 24443160 DOI: 10.1002/mrm.25074]

P- Reviewer: Can M, Izawa KP, Kirali K S- Editor: Ji FF

L- Editor: A E- Editor: Lu YJ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

