Reducing Radiation in Chronic Total Occlusion Percutaneous Coronary Interventions

Antonis N. Pavlidis*[1], Daniel A. Jones[1], Alex Sirker[2], Anthony Mathur[1] and Elliot J. Smith[1]

[1]*Department of Cardiology, London Chest Hospital, Barts Health NHS Trust, London, UK;* [2]*Department of Cardiology, The Heart Hospital, University College London Hospitals NHS Foundation Trust, London, UK*

A.N. Pavlidis

Abstract: The field of percutaneous intervention for chronic total occlusion (CTO) has enjoyed significant innovations in the recent years. Novel techniques and technologies have revolutionized the field and have resulted in considerably higher success rates even in patients with high anatomical complexity. Successful CTO recanalization is associated with significant clinical benefits, such as the improvement of angina and quality of life, reduced rates of surgical revascularization, improvement of left ventricular function and decreased mortality rates. However, complex CTO procedures often require prolonged x-ray exposure which have been associated with adverse long term outcomes.

Keywords: Coronary artery disease, chronic total occlusions, coronary intervention, radiation, skin injury.

INTRODUCTION

Radiation exposure is higher during percutaneous coronary interventions (PCI) for chronic total occlusions (CTO) compared to non-CTO interventions because of prolonged fluoroscopic time and repeated cine angiography [1]. Although radiation skin injury is rare, the risks of radiation-related complications are greater in CTO procedures. Moreover, operator and lab staff exposure can result in longterm adverse outcomes, such as cataracts and malignancies, therefore reducing radiation exposure is a key factor in CTO interventions.

RADIATION DOSES IN CTO PROCEDURES

There are three different values that are currently measured by modern interventional fluoroscopic equipment: (a) the *entrance surface air kerma (ESAK)*, measured in Gray (Gy), which represents the radiation energy released at the point where the X-ray beam enters the patient's skin surface and includes both the incident air kerma and radiation backscattered from the tissue, (b) the *dose area product (DAP)*, measured in $Gy.cm^2$, which represents the product of the dose in air within the X-ray beam and the beam area, and is therefore a measure of all the radiation that enters the patient and (c) the *fluoroscopic time (FT)*, measured in minutes, which is the time during a procedure that fluoroscopy is used. The ESAK is used to measure the deterministic risk to the patient such as skin injury, while the DAP is used to measure the stochastic risk of the patient, which involves the likelihood of developing malignancies or genetic defects in the future. FT does not include cine acquisition imaging and is therefore inadequate to assess patient radiation.

A plain chest radiography produces a DAP of 0.08 $Gy.cm^2$ with a background equivalent of three days, while the equivalents for a non-CTO PCI with one stent are 36 $Gy.cm^2$ and 3.7 years [2]. According to a study by Suzuki *et al*. [1] the median ESAK for a CTO PCI was 4.6 Gy, compared to 2.4 Gy, 1.5 Gy and 1.2 Gy for multivessel, single-vessel multiple stenosis and single stenosis PCI respectively.

Several lesion- and patient-related risk factors have been shown to affect radiation dose during percutaneous interventions. In a study of 1933 PCI procedures Fetterly *et al*. [3] found that lesion complexity, PCI of left circumflex artery, previous coronary artery bypass grafting (CABG), body mass index (BMI) and the number of treated lesions correlated to an increased ESAK. Similar results were found in a larger study by Delewi *et al*. [4] which included 9850 PCI procedures. They demonstrated that high BMI, previous history of coronary artery bypass grafting, the number of treated lesions and CTO interventions were associated with the highest patient radiation exposure.

DETERMINISTIC EFFECTS

Radiation-induced skin injury is an infrequent complication during PCI, but appears more often in CTO interventions as a result of prolonged fluoroscopy times. Radiation toxicity is rare with <5 Gy but patients with higher doses should be followed up 2-3 weeks after the procedure and assessed for development of new skin changes. At Grade I radiation-induced skin injury a faint erythema can be seen during the first 48 hours after exposure. Following a latent phase that can last up to 5 weeks, moderate to brisk erythema with oedema can be observed. Larger doses of radiation can result in Grade IV injury with skin necrosis or ulceration within 2 weeks after exposure (Fig. **1**), (Table **1**) [5].

*Address correspondence to this author at the Cardiology Department, London Chest Hospital, Bonner Road, London, UK E2 9JX; Tel: +4407500452700: E-mail: antonispav@yahoo.com

1573-403X/16 $58.00+.00

(Source http://www.fda.gov/radiation-emittingproducts)

Fig. (1). Radiation-induced skin injury.

Radiation-induced skin injury appears to be the least frequently reported complication following CTO intervention. In a meta-analysis of 65 studies Patel *et al*. [6] showed an incidence of <0.01% with only 3 reported cases among 2,857 patients. However, radiation skin injury was the least frequently reported CTO complication, with only 11% of the studies reporting on its occurrence. In another metanalysis of retrograde CTO interventions, El Sabbagh *et al*. [7] reported an incidence of 0.5%, although only 2 out of the 26 studies (0.08%) reported this complication. Morino *et al*. [8] published the outcomes for 498 patients and 528 CTO lesions included in the J-CTO registry (Multicenter CTO Registry of Japan) and no incidents of radiation-induce skin injuries were reported. The incidence of radiation skin in the most recent CTO registries and meta-analyses is summarised in Table **2**.

STOCHASTIC EFFECTS

Radiation dose exposure has been related to an additional risk of developing solid tumours [9]. The Biological Effects of Ionizing Radiation (BEIR) VIII risk model suggests that the risk of malignancy increases proportionally to the dose of the radiation, with no low-dose threshold [10]. At low doses of exposure, the risk of developing a malignancy is naturally low, but not zero. Minimal data on the risk of malignancy related to radiation exposure during PCI are available. Godino *et al*. [11] estimated the malignancy risk due to radiation

Table 1. Staging of radiation skin injury [31].

Grade	Skin appearance	Radiation dose	Time after radiation exposure
1	Faint erythema or desquamation	> 2 Gy	First 48 hours
2	Moderate to brisk erythema or moist desquamation. Moderate swelling.	> 15 Gy	2-5 weeks
3	Confluent, moist desquamation > 1.5 cm diameter, which is not confined to the skin folds. Pitting oedema	> 40 Gy	6-7 weeks
4	Skin necrosis or ulceration of full thickness dermis	> 550 Gy	2 weeks

Table 2. Radiation doses in recent CTO registries and meta-analyses.

	Study type	Characteristics	Year	CTO lesions (n)	Radiation skin injury (%)	Fluoroscopy time
Lin *et al*. [32]	Retrospective study		2014	516	NR	43 ± 27 [#] 42 ± 24 [##]
El Sabbagh *et al*. [7]	Metanalysis	Retrograde only	2014	3493	0.5%	82 ± 34
Christopoulos *et al*. [33]	Registry		2014	496	NR	41 (26-65) *
Michael *et al*. [34]	Registry		2013	1361	NR	42 ± 29
Karmpaliotis *et al*. [35]	Registry	Retrograde only	2012	462	NR	61 ± 40
Tsuchikane *et al*. [36]	Registry	Retrograde only	2013	801	NR	95 ± 52
Patel *et al*. [37]	Metanalysis		2013	18941	<0.01	NR
Galassi *et al*. [38]	Registry		2011	1983	NR	42 ± 47
Morino *et al*. [8]	Registry		2010	528	0	45 (1-301) *
Aguiar-Souto *et al*. [39]	Retrospective study		2010	227	NR	32 (19-47) *

[#]CI-AKI group, [##] non CI-AKI group, CI-AKI: contrast induced acute kidney injury, * Median (range) exposure in patients undergoing PCI for acute ST-elevation myocardial infarction (STEMI) and patients undergoing CTO PCI by incorporating the effective radiation dose into the Biological Effects of Ionizing Radiation (BEIR) VII model [12]. They found that the number of estimated additional lung and bone marrow malignancy cases were on average two times higher in patients treated for CTOs compared to STEMI patients. Nevertheless, the above observations have not yet been confirmed in epidemiological studies and there is therefore insufficient evidence to defer a CTO intervention based on concerns over radiation exposure [13].

RADIATION EXPOSURE EFFECTS TO OPERATORS

Chronic exposure to low doses of ionising radiation has shown to cause DNA damage in interventional cardiologists, which appears to correlate with the number of years of catheterization laboratory experience [14]. Venneri *et al.* [15] used the BEIR VII model to show that interventionalists had an increased cancer risk caused by professional radiation exposure. Recently published case clusters of interventional cardiologists with left sided brain neoplasms have raised the existing concerns, since radiation exposure to the left side is higher during PCI [16-18]. Despite the above, the risks related to radiation exposure in operators remains uncertain and further studies are required.

Radiation-induced cataracts represents another occupational hazard to interventional cardiologists. The RELID (Retrospective evaluation study of lens injuries and dose) study showed that they have a three-fold higher rate of posterior subcapsular lens opacities compared to unexposed individuals. Although the risk of developing cataracts is dose-dependent [19], it appears to be lower for regular users of protective lead glasses [20]. The International Commission on Radiological Protection (ICRP) have suggested a threshold dose to the lens of 20 mSv per year, averaged over 5 consecutive years, with a maximum of 50 mSv in a single year [21].

METHODS FOR REDUCING RADIATION DURING CTO INTERVENTIONS

A). Pre-procedural Strategies

Careful selection of patients and early assessment of the risk factors that are associated with high risk for radiation injury is of primary importance. Patients with recent radiation exposure are at particularly high risk of radiation skin injury [22]. Every patient should be consented on the risks of radiation-related complications and careful examination of the skin should be performed prior to starting a CTO procedure. Moreover, the ‘CTO team’, including physicians, nurses and technicians, should always review the angiographic images prior to the procedure in order to understand the anatomy and plan the interventional strategy. Specific radiographic views that are most likely to be useful should be identified early in order to avoid unnecessary radiation exposure.

Computed tomography coronary angiography (CTCA) is a useful tool for CTO pre-procedural planning. Although the contribution of multislice CT (MSCT) is approximately 19 mSv [23] the total radiation dose can be decreased significantly with successful CTO road mapping, based on the additional information on lesion characteristics. Incorporation of ECG-pulsed modulation of the tube current [24] and the use of new generation MSCT equipment can lower the effective radiation dose significantly [2].

Finally, each cardiac lab should have an established radiation safety program and operators should undergo compulsory training on radiation dose management and safety. Studies have shown that radiation doses can be reduced up to 34% if operators have recently attended an informative conference on appropriate use of radiation and changes in x-ray delivery settings [25].

B). Intra-procedural Strategies

Staff radiation dose should be closely monitored with personal dose monitors and dosimeter records should be provided to operators regularly. The ICRP recommends the use of two dosimeters [21]: one under the protective garment, usually at waist height, and a second outside the thyroid collar. If unusually high doses are recorded a review of staff practice patterns and adoption of further safety measures should be applied.

Protective 0.5 mm lead aprons, thyroid shielding, shin leg covers and radiation-specific glasses can stop up to 95% of the scattered radiation and should be worn by all CTO operators [22]. Apart from the commonly used radiation shielding, additional protection could be achieved during CTO interventions with below table mounted shielding and the recently developed Trinity Radiation Protection system [26]. The latter consists of a combination of fixed shields, radiation drapes and interconnecting flexible radiation resistant materials that create a complete radiation protection environment for the operators.

All CTO operators should be familiar with and apply the ALARA (As Low As Reasonably Achievable) principle, which means using all relevant methods and strategies in order to minimize radiation dose. Radiation exposure should be closely monitored at any time during the procedure. The operator should be alerted by the cardiac lab team when radiation levels exceed certain limits in order to balance the risks and benefits of discontinuing the procedure. A dose of 10 Gy ESAK has been suggested as a threshold at which a CTO operator should discontinue the procedure provided it is safe to do so, unless lesion crossing has occurred and the procedure is expected to be completed within a short period of time [27].

Increasing the distance between the patient and the X-ray tube by positioning the table at a higher level can result in significant reduction of radiation dose, although this should never affect the operator’s comfort [28]. Higher magnification increases the patient’s dose and should only be utilized in special circumstances. Moreover, all CTO operators should be familial with undergoing procedures at lower framing rates per second (fps) (6.0-7.5 fps instead of 15 fps) and using pulsed fluoroscopy mode rather than the digital cine mode storage. The number of acquisition runs should be held for optimising the strategy and assessing possible complications. Altering the beam angulation during the procedure by rotating the x-ray tube more than 40° can reduce the patient's skin dose and minimize irradiation of a particular portion of the patient's skin [29, 30]. Steep angles have been linked to higher radiation doses due to penetration through more layers of tissue and should therefore be avoided [28]. Collimation decreases scatter radiation and the overall dose received by the patient. The use of additional copper filters reduces primary beam exposure and can enhance focused visualization.

CTO SPECIFIC TECHNIQUES

Adoption of the hybrid approach with early switch from a failing strategy maximizes the chance of procedural success, reduces procedure time and minimises radiation [27]. Although there are no specific time limits for each of the algorithm steps, operators should stop pursuing a technique that has not resulted in any significant progress during a reasonable period of time [27].

The use of certain techniques during CTO interventions can result in significant reduction of total radiation exposure:

- The trapping technique for equipment exchange (balloon inflation inside the guiding catheter to fix the wire).
- During dual injections, the donor vessel is injected first to allow time to fill the distal vessel. Fluoroscopy or cine acquisition begins 1-2 seconds later and it is followed by injection of the occluded vessel.
- The use of intravascular ultrasound (IVUS) for proximal cap identification, re-entry guidance, assessment of retrograde wire position in reverse CART and stent optimisation.
- Marking the length of the wire that can be advanced safely without exiting the microcatheter during wire exchanges or when modifying the wire's tip bend. A pre-attached torquer at the end of the inserted wire or a stable marker on the table can be used.

The methods for reducing radiation during CTO interventions are summarised in Table **3**.

C). Post-procedural Strategies and Follow Up

Post-procedure dose analysis is important in order to determine further management and follow up, especially if a repeat procedure is planned and the initial procedure resulted in high radiation exposure. The CTO procedure report should include all available radiation dose parameters, such as the fluoroscopy time, ESAK and DAP.

Post-procedure follow up should be guided by the Air Kerma Dose that the patient received during the CTO intervention [22]:

- **5 Gy:** patients should be educated regarding potential skin changes on their back. A thorough examination of the skin should be performed 1 month following the procedure and if there is evidence of radiation-induced skin injury an appropriate specialist referral should be considered.
- **10 Gy:** patients should be educated accordingly and followed up after 2-4 weeks. A qualified physicist should promptly be asked to calculate peak skin dose.
- **15 Gy:** dosed above this level are identified by the Joint Commission as a sentinel event, therefore hospital risk management and regulatory authorities need to be contacted within 24 hours after the procedure. No interventional procedure should reach this level unless there is a life threatening complication that necessitates obligatory percutaneous fluoroscopic reversal.

CONCLUSIONS

The field of CTO-PCI has evolved significantly in recent years and the hybrid approach to CTO offers the opportunity to treat more complex anatomy successfully and meet the needs of a wider patient population. Prevention of complications related to use of radiation represents a major compo-

Table 3. Methods for reducing radiation during CTO interventions.

Pre-procedure	Intra-procedure	Post-procedure
Patient selection and risk assessment	Dosimeters	Dose documentation
Consent	Protection clothing	Follow up
Review films	Shielding	
CTCA	ALARA principle	
Radiation safety program	Alert operator when radiation exceeds limits	
Compulsory training on radiation safety and management	Table position at higher level	
	Lower magnification	
	Lower frame rates	
	Changing beam angulation	
	Collimation	
	Procedure techniques	

CTO: chronic total occlusion, CTCA: computed tomography coronary angiography, ALARA: As Low As Reasonably Achievable nent of a successful CTO intervention. Operator awareness and use of all the required precautions improves patient, staff and physician safety.

FUNDING

This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Suzuki S, Furui S, Kohtake H, *et al.* Radiation exposure to patient's skin during percutaneous coronary intervention for various lesions, including chronic total occlusion. Circ J 2006; 70: 44-8.
[2] Sianos G, Werner GS, Galassi AR, *et al.* Recanalisation of chronic total coronary occlusions: 2012 consensus document from the EuroCTO club. EuroIntervention 2012; 8: 139-45.
[3] Fetterly KA, Lennon RJ, Bell MR, Holmes DR Jr, Rihal CS. Clinical determinants of radiation dose in percutaneous coronary interventional procedures: influence of patient size, procedure complexity, and performing physician. JACC Cardiovasc Interv 2011; 4: 336-43.
[4] Delewi R, Hoebers LP, Råmunddal T, *et al.* Clinical and procedural characteristics associated with higher radiation exposure during percutaneous coronary interventions and coronary angiography. Circ Cardiovasc Interv 2013; 6: 501-6.
[5] Slovut DP. Cutaneous radiation injury after complex coronary intervention. JACC Cardiovasc Interv 2009; 2: 701-2.
[6] Patel VG, Michael TT, Mogabgab O, *et al.* Clinical, angiographic, and procedural predictors of periprocedural complications during chronic total occlusion percutaneous coronary intervention. J Invasive Cardiol 2014; 26: 100-5.
[7] El Sabbagh A, Patel VG, Jeroudi OM, *et al.* Angiographic success and procedural complications in patients undergoing retrograde percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 3,482 patients from 26 studies. Int J Cardiol 2014; 174: 243-8.
[8] Morino Y, Kimura T, Hayashi Y, *et al.* In-hospital outcomes of contemporary percutaneous coronary intervention in patients with chronic total occlusion insights from the J-CTO Registry (Multicenter CTO Registry in Japan). JACC Cardiovasc Interv 2010; 3: 143-51.
[9] Wrixon AD. New ICRP recommendations. J Radiol Prot 2008; 28: 161-8.
[10] Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA 2007; 298: 317-23.
[11] Godino C, Maccagni D, Pavon AG, *et al.* Estimating incidence of organ cancer related to PCI radiation exposure in patients treated for acute and chronic total occlusions. J Invasive Cardiol 2013; 25: 441-5.
[12] Committee to Assess Health Risks from Exposure to Low Level of Ionizing Radiation. Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2: Washington, DC: National Academies; National Research Council.
[13] Shah N, Deshmukh A, Sachdeva R. Radiation exposure after percutaneous coronary intervention: is the cancer risk real? J Invasive Cardiol 2013; 25: 447-8.
[14] Andreassi MG, Cioppa A, Botto N, *et al.* Somatic DNA damage in interventional cardiologists: a case-control study. FASEB J 2005; 19: 998-9.
[15] Venneri L, Rossi F, Botto N, *et al.* Cancer risk from professional exposure in staff working in cardiac catheterization laboratory: insights from the National Research Council's Biological Effects of Ionizing Radiation VII Report. Am Heart J 2009; 157: 118-24.
[16] Roguin A, Goldstein J, Bar O. Brain tumours among interventional cardiologists: a cause for alarm? Report of four new cases from two cities and a review of the literature. EuroIntervention 2012; 7: 1081-6.
[17] Roguin A, Goldstein J, Bar O. Brain malignancies and ionising radiation: more cases reported. EuroIntervention 2012; 8: 169-70.
[18] Roguin A, Goldstein J, Bar O, Goldstein JA. Brain and neck tumours among physicians performing interventional procedures. Am J Cardiol 2013; 111: 1368-72.
[19] Ciraj-Bjelac O, Rehani MM, Sim KH, Liew HB, Vano E, Kleiman NJ. Risk for radiation-induced cataract for staff in interventional cardiology: is there reason for concern? Catheter Cardiovasc Interv 2010; 76: 826-34.
[20] Jacob S, Boveda S, Bar O, *et al.* Interventional cardiologists and risk of radiation-induced cataract: results of a French multicenter observational study. Int J Cardiol 2013; 167: 1843-7.
[21] International Commission on Radiological Protection. Avoidance of radiation injuries from medical interventional procedures. Ann ICRP 2000; 25-43.
[22] Chambers CE, Fetterly KA, Holzer R, *et al.* Radiation safety program for the cardiac catheterization laboratory. Catheter Cardiovasc Interv 2011; 77: 546-56.
[23] García-García HM, van Mieghem CA, Gonzalo N, *et al.* Computed tomography in total coronary occlusions (CTTO registry): radiation exposure and predictors of successful percutaneous intervention. EuroIntervention 2009; 4: 607-16.
[24] Abada HT, Larchez C, Daoud B, Sigal-Cinqualbre A, Paul JF. MDCT of the coronary arteries: feasibility of low-dose CT with ECG-pulsed tube current modulation to reduce radiation dose. AJR Am J Roentgenol 2006; 186: S387-90.
[25] Azpiri-López JR, Assad-Morell JL, González-González JG, *et al.* Effect of physician training on the X-ray dose delivered during coronary angioplasty. J Invasive Cardiol 2013; 25: 109-13.
[26] Fattal P, Goldstein JA. A novel complete radiation protection system eliminates physician radiation exposure and leaded aprons. Catheter Cardiovasc Interv 2013; 82: 11-6.
[27] Brilakis ES, Grantham JA, Rinfret S, *et al.* A percutaneous treatment algorithm for crossing coronary chronic total occlusions. JACC Cardiovasc Interv 2012; 5: 367-79.
[28] Brilakis ES, ed. Manual of Coronary Chronic Total Occlusion Interventions. A Step-By-Step Approach. Waltham, MA: Elsevier; 2013.
[29] Abdelaal E, Plourde G, MacHaalany J, *et al.* Effectiveness of low rate fluoroscopy at reducing operator and patient radiation dose during transradial coronary angiography and interventions. JACC Cardiovasc Interv 2014; 7: 567-74.
[30] Bashore TM, Balter S, Barac A, *et al.* 2012 American College of Cardiology Foundation/Society for Cardiovascular Angiography and Interventions expert consensus document on cardiac catheterization laboratory standards update: A report of the American College of Cardiology Foundation Task Force on Expert Consensus documents developed in collaboration with the Society of Thoracic Surgeons and Society for Vascular Medicine. J Am Coll Cardiol 2012; 59: 2221-305.
[31] Bernier J, Bonner J, Vermorken JB, *et al.* Consensus guidelines for the management of radiation dermatitis and coexisting acne-like rash in patients receiving radiotherapy plus EGFR inhibitors for the treatment of squamous cell carcinoma of the head and neck. Ann Oncol 2008; 19: 142-9.
[32] Lin YS, Fang HY, Hussein H, *et al.* Predictors of contrast-induced nephropathy in chronic total occlusion percutaneous coronary intervention. EuroIntervention 2014; 9: 1173-80.
[33] Christopoulos G, Menon RV, Karmpaliotis D, *et al.* Application of the "hybrid approach" to chronic total occlusions in patients with previous coronary artery bypass graft surgery (from a Contemporary Multicenter US registry). Am J Cardiol 2014; 113: 1990-4.
[34] Michael TT, Karmpaliotis D, Brilakis ES, *et al.* Procedural outcomes of revascularization of chronic total occlusion of native coronary arteries (from a multicenter United States registry). Am J Cardiol 2013; 112: 488-92.
[35] Karmpaliotis D, Michael TT, Brilakis ES, *et al.* Retrograde coronary chronic total occlusion revascularization: procedural and in-hospital outcomes from a multicenter registry in the United States. JACC Cardiovasc Interv 2012; 5: 1273-9.

[36] Tsuchikane E, Yamane M, Mutoh M, *et al*. Japanese multicenter registry evaluating the retrograde approach for chronic coronary total occlusion. Catheter Cardiovasc Interv 2013; 82: E654-61.

[37] Patel VG, Brayton KM, Tamayo A, *et al*. Angiographic success and procedural complications in patients undergoing percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 18,061 patients from 65 studies. JACC Cardiovasc Interv 2013; 6: 128-36.

[38] Galassi AR, Tomasello SD, Reifart N, *et al*. In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion: insights from the ERCTO (European Registry of Chronic Total Occlusion) registry. EuroIntervention 2011; 7: 472-9.

[39] Aguiar-Souto P, Ferrante G, Del Furia F, Barlis P, Khurana R, Di Mario C. Frequency and predictors of contrast-induced nephropathy after angioplasty for chronic total occlusions. Int J Cardiol 2010; 139: 68-74.

Received: November 08, 2014 Revised: January 13, 2015 Accepted: January 16, 2015