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Detection and quantification of human immunodeficiency virus and hepatitis C virus in cadaveric tissue donors using different molecular tests

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ABSTRACT

Background: Tissues from cadaveric donors are used in several clinical circumstances, and the transmission of infectious diseases has been reported. Cadaveric donor (CD) blood sample analysis is challenging due to its poor quality. However, studies have demonstrated the usefulness of molecular based methods, and the lack of studies using available commercial molecular tests was reported.
Objective: The aim of this study was to evaluate the performance, specificity, sensitivity, and accuracy of different commercial molecular tests for HIV and HCV detection and quantification in CD through spiked samples.
Study design: 20 CD and 20 blood donor samples were tested using 1,000 copies/mL and 1,000 IU/mL of lyophilized standards of HIV and HCV, respectively. Samples were analyzed by different molecular kits: XPERT HCV Viral Load and HIV-1 (Cepheid), COBAS® TaqMan® HIV-1 and COBAS® TaqMan® HCV Test, v2.0 (Roche), and artus® HI Virus-1 QS-RGQ and artus® HCV RG RT-PCR Kit (Qiagen).
Results: HIV and HCV in CD were detected by RT-PCR-based quantitative kits. The tests performed by the Cepheid and the Roche kits showed the most accurate, sensitive and specific results, however, a wide variability between the assays and kits was observed. The Qiagen kits did not demonstrate satisfactory results.
Conclusions: CD evaluation showed great variability. The Cepheid and Roche kits were more sensitive for detecting HIV on CD and Cepheid was the most efficient kit for HCV quantification in CD. The Roche and Cepheid kits can be used to screen tissue donors for HIV and HCV.

1. Background

Tissue banks evaluate potential donors with several serological screening tests for infectious diseases. These tests can vary according to the tissue and the patient's origin, including risk for endemic infectious diseases [1–5]. Despite the rigorous microbiological and viral screening of tissue donors, transmission of infectious diseases has been reported [6–10], such as cytomegalovirus, rabies, prion disease, hepatitis B virus, hepatitis C virus (HCV), and human immunodeficiency virus (HIV).

Several analytical methods can be performed in tissue donors samples for HIV and HCV diagnosis, including testing for antibodies, antigens and nucleic acids (NAT) [4,11–14]. All these tests are specific and sensitive; however, NAT and other molecular-based methods can detect the viruses sooner than antibody and antigen tests, increasing the safety of the donated tissues [4,5,15–18].Cadaveric serum and plasma specimens are usually collected after circulation and are often of poor quality. This is due to effects of hemolysis, hemodilution, autolysis, bacterial growth, and other factors, which can interfere in immunological tests (antigen and antibody) [18].

2. Objectives

Considering the shortage of available tests for cadaveric specimens that are developed, validated for use and standardized in Brazil, the aim of this study was to evaluate the specificity, sensitivity, and accuracy of different commercial molecular tests for the detection and quantification of HIV and HCV in peripheral blood samples from cadaveric donors through spiked samples.

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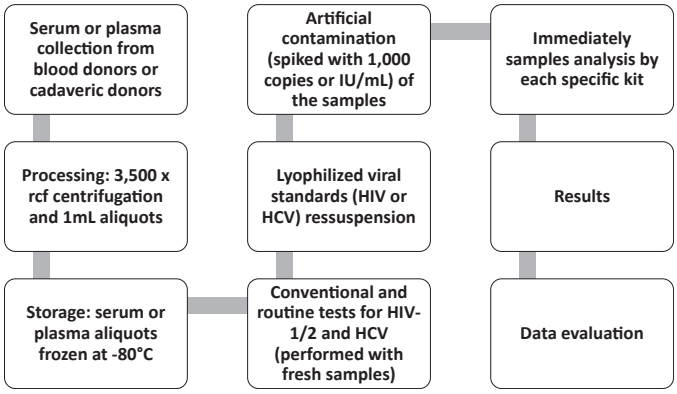

Fig. 1. Processing scheme of samples (of both groups – blood and cadaveric donors).

3. Study design

3.1. Experimental study design

The definition of cadaveric tissue donors used the Brazilian criteria established by regulatory agencies [19]. This study was approved by the Ethics Committee of Pontifícia Universidade Católica do Paraná (approval number 83,139,718.5.0000.0020). All samples were obtained after donor or family authorization. A total of 20 samples from cadaveric donors and 20 samples from blood donors were collected from April/2018 to October/2018 and stored at −80 °C until testing (Fig. 1).

3.2. Sample collection, storage and organization

Peripheral blood samples from 20 cadaveric tissue donors were collected (after authorization) into serum tubes (Vacutainer®, BD Biosciences, San Jose, CA, USA) and in EDTA K2 tubes for plasma (Vacutainer®, BD Biosciences, San Jose, CA, USA). In this group, 20 samples were spiked with 1000 copies/mL HIV, 20 samples were spiked with 1000 IU/mL HCV, and 10 samples were not spiked and used as negative controls for both HIV (5 samples) and HCV (5 samples). For HIV tests, only the plasma aliquots were used, while the HCV tests were performed using serum aliquots (except when using Qiagen kits, which used plasma for both tests, see below).

In addition, peripheral blood samples from 20 blood donors were collected after informed consent. The peripheral blood samples were collected into serum and plasma tubes. In this group, 10 samples were spiked with HIV, 10 samples were spiked with HCV, and, as above, 10 samples were not spiked and used as negative controls for both HIV (5 samples) and HCV (5 samples). For HIV tests, only plasma aliquots were used, while HCV tests were performed with serum aliquots (except for Qiagen kits, which used plasma for both tests, see below).

For both groups (cadaveric and blood donors), the tubes were homogenized according to the manufacturer's recommendation and centrifuged at 3500 × *g* for 15 min at room temperature, according to Gubbe et al. [14]. One mL aliquots were stored at −80 °C. Fresh samples (immediately processed and analyzed after collection) from both groups were previously tested for HIV and HCV by two distinct standardized routine serological methodologies (immunoenzymatic assays, 4th generation) and NAT, with the aim of excluding contaminated samples (Fig. 1).

3.3. Characteristics of molecular detection kits

Tests were performed according to the manufacturer's instructions for use (IFU), using six different kits commercialized in Brazil. XPERT HCV Viral Load (Cepheid, Sunnyvale, CA, USA), XPERT HIV-1 (Cepheid, Sunnyvale, CA, USA), COBAS® TaqMan® HIV-1 Test, v2.0 (Roche, Meylan, France), COBAS® TaqMan® HCV Test, v2.0 (Roche, Meylan, France), artus® HI Virus-1 QS-RGQ (Qiagen, Hamburg, Germany) and artus® HCV RG RT-PCR Kit (Qiagen, Hamburg, Germany). The IFU do not include instructions for specimen collection, storage and handling of cadaveric specimens.

3.4. Spiking technique using viral standards from National Institute and biological standards and control (NIBSC)

Viral lyophilized standards of HIV-1 RNA 16/194 (NIBSC/WHO/2017) and HCV NAT 14/150 (NIBSC/WHO/2016) were diluted with molecular grade water (Invitrogen, Carlsbad, CA, USA), according to their respective IFU. Each standard was then aliquoted and stored at −80 °C until use (Fig. 1).

The samples of plasma or sera for each group were contaminated with 1000 copies/mL of HIV-1 and 1000 IU/mL of HCV, separately. They were then immediately tested using the detection protocol described below (Fig. 1).

3.5. Detection protocol using molecular detection

All tests were performed strictly according to the IFU. All kits used the methodology based on PCR tests. Interpretation of the results was done using the software for each kit. In addition to the spiked and negative samples, internal, positive and negative controls were evaluated in each reaction to validate the reaction, according to IFU.

Sample characteristics and clinical data from each donor were collected and evaluated. These included: hemolysis none, + (mild), + + (moderate) and + + + (severe), hemodilution, fibrin clot, gender, age, hospital of origin, city, state, use of antibiotics, cause of death, comorbidities, presence of infection, day and time of death, and time of sample collection.

3.6. Statistical analyses

Results were compiled and analyzed using mean, standard deviation (SD) and Cohen's kappa coefficient (κ), which was calculated to measure inter-rater agreement for qualitative (categorical) items. Fisher's exact test was performed to correlate the sample quality and assay results. The evaluation of operational characteristics of the PCR-based tests was made through a comparison of the results obtained using the different kits. Sensitivity, specificity and accuracy were calculated. Moreover, the Student's *t*-test and *p* value concordance were also calculated with GraphPad Prism 7 (GraphPad Prism Software Inc., San Diego, USA).

4. Results

4.1. Cadaveric donors'and samples' characteristics

Among the cadaveric donor samples, some showed hemolysis + (n = 7), lipemic characteristic (n = 1) and fibrin clots (n = 3). Twelve patients were under antibiotic therapy; but sepsis or active bacterial infection was diagnosed in only 6 donors. In two donors, hemodilution (increased plasma volume in relation to red cells) was detected, one donor presented increased bilirubin, and one donor had a positive HTLV serology. None of these factors were associated with tests results (invalidity, positive or negative results, $p > 0.05$). The mean time difference between death and sample collection was 03:37 h, ranging from 01:05 h to 11:14 h. The cadaveric donors' mean age was 51.5 years old, ranging from 8 to 77 years old. In addition, 55% of donors were men. Twenty five percent of donations were heart (for valves), 75% the cornea, 10% bones, and 5% skin. Samples collected from blood donors had no alterations (such as hemolysis, lipemic characteristic, or fibrin clots). Among the samples, 60% were from women, while 40% were from men. All donor specimens tested for HIV-1/2 and HCV using two distinct serological methodologies (immunoenzymatic assays, 4th generation) and routine NAT prior to using the specimen for the study, and one blood donor had HCV reactivity with serological methodologies, being excluded from the study.

4.2. HIV molecular detection kits evaluation

When analyzing Cepheid's XPERT HIV-1, 19 out 20 samples from cadaveric donors had virus detected and the viral load quantified, with a mean quantification of 2.83 log (SD 0.13) and 703.95 copies/mL (SD 216.15). Only one sample had an invalid result (unable to obtain result), indicating that some factor inhibited the reaction. For the same kit, 10 out 10 samples from blood donors were able to have the viral load quantified, with a mean quantification of 2.80 log (SD 0.04) and 629.60 copies/mL (SD 68.75). None of the negative controls from cadaveric donors had virus detected, demonstrating 100% specificity. In addition, the accuracy of this test for cadaveric samples spiked with HIV was 96% (Table 2).

For Roche's COBAS® TaqMan® HIV-1 Test, v2.0, HIV was detected and quantified in all samples from cadaveric donors, with a mean quantification of 2.41 log (SD 0.16) and 274.60 copies/mL (SD 90.10). For the same kit, all samples from blood donors were quantified, and had a viral load with a mean quantification of 2.25 log (SD 0.13) and 186.50 copies/mL (SD 55.08). None of the negative controls from cadaveric donors showed amplification of virus, demonstrating 100% specificity. Additionally, the accuracy of this test for cadaveric samples spiked with HIV was 100% (Table 2).

Qiagen's artus® HI Virus-1 QS-RGQ had a mean quantification of 2.63 log (SD 0.52) and 690 copies/mL (SD 603.49) for cadaveric donor samples. However, 6 out the 20 samples were invalid and 4 did not have virus detected. In the negative controls, 3 were invalid and 2 did not have virus detected. For the blood donors, all samples had virus detected, with a mean quantification of 2.82 (SD 0.25) and 750 copies/mL (SD 382.88). Moreover, all the negative controls did not have virus detected. Due to the invalid results on the negative controls from cadaveric samples, the test specificity was 40%. In addition, the accuracy of this test for cadaveric samples spiked with HIV was 48% (Table 2).

Comparing the quantitative results, the tests showed distinct results with a statistical difference between Roche vs. Qiagen ($p = 0.0028$) and between Roche vs. Cepheid ($p = 0.0002$). When comparing Qiagen vs. Cepheid, no significant difference was observed ($p = 0.9925$). Furthermore, the same analysis for blood donor samples demonstrated a significant difference between Roche vs. Qiagen ($p \leq 0.0001$) and Roche vs. Cepheid ($p = 0.0005$), however, Qiagen vs. Cepheid showed no significant difference ($p = 0.4710$) (Fig. 2).

Regarding the qualitative results, an almost perfect agreement was observed between Cepheid and Roche, while a slight agreement could be observed between Cepheid- and Roche vs. the Qiagen kits (Table 1).

4.3. HCV molecular detection kits evaluation

The Cepheid's XPERT HCV Viral Load could quantify all 20 cadaveric donor samples, reporting a mean quantification of 2.50 log (SD 0.17) and 343.35 IU/ml (SD 134.36), 100% accuracy and 100% sensitivity. Blood donors' samples showed 10 out 10 detection with a mean quantification of 2.51 log (SD 0.12) and 333.60 IU/ml (SD 84.29). None of the negative controls from cadaveric samples had virus detected, demonstrating 100% specificity (Table 2).

The Roche's COBAS® TaqMan® HCV Test, v2.0 showed a mean quantification of 2.62 log (SD 0.30) and 501.11 IU/ml (SD 308.96) for cadaveric donor samples, however, 2 out of the 20 samples showed no detection of virus and 2 out 20 samples showed an invalid result. Moreover, 2 out 5 negative controls showed an invalid result, demonstrating 60% specificity, 80% sensitivity and 76% accuracy. For the blood donor samples, all showed quantification with a mean of 2.53 log (0.51) and 571.28 IU/ml (SD 560.03). All negative control samples did not have virus detected (Table 2).

For the Qiagen's artus® HCV RG RT-PCR Kit, the cadaveric spiked donor samples showed that 8 were invalid and 12 did not have virus detected, while the negative controls showed that 4 were invalid and 1 did not have virus detected, demonstrating that the test had 0% accuracy, 20% specificity and 0% sensitivity (Table 2). For spiked blood donor samples, the mean quantification was 2.68 log (SD 0.20) and 528 IU/ml (SD 241.33), and all negative controls did not have virus detected.

The tests between brands showed no significant difference when comparing Cepheid vs. Roche ($p = 0.4104$). Furthermore, the same analysis for blood donor samples demonstrated no significant difference among the brands; Roche vs. Qiagen ($p = 0.9600$), Roche vs. Cepheid ($p = 0.3090$) and Qiagen vs. Cepheid ($p = 0.4502$) (Fig. 3) (Fig. 3).

5. Discussion

HIV and HCV in cadaveric samples could be detected by PCR-based quantitative kits, and the tests performed by Cepheid and Roche showed the most accurate, sensitive and specific results. However, a wide variability between the tests and kits quantification was found. Blood donor samples showed less variability than the cadaveric ones when HIV was tested. These samples also showed no inhibition or false-negative results. The Qiagen kit showed wider variability than the other kits for HIV.

Quantitative molecular-based methods showed that the turnaround time is short, and it is possible using these methods when using approximately 1000 copies or IU/ml. Complementary to these data, our results with the different assays performed in this study have demonstrated good agreement between tests [20–22]. Cadaveric samples are known to contain inhibitory factors that may lead to invalid or false-negative results. These include: hemodilution, increased bilirubin, hemolysis, sepsis or active bacterial infection and viral detection and may affect the reaction [23–25]. Similar results were observed in this study comparing kits and samples quality, where altered cadaveric samples showed invalid results. Qualitative and quantitative tests using living donors and clinical samples are reported using different tests and approaches. Amendola et al., 2014 have demonstrated the ability of two commercially available assays to quantify low levels of HIV-1 RNA, using clinical and spiked samples from living donors [26], and the results of this work showed high accuracy and sensitivity, being able to detect as low as 3.5 copies/mL of HIV-1 RNA with 95% of probability.

Moreover, a study for HCV RNA quantification using human plasma and serum and NIBSC standards showed robust and reliable assays, exhibiting high sensitivity and specificity [28]. Invalid results were more frequent in HCV kits; however, they also occur in HIV kits. The

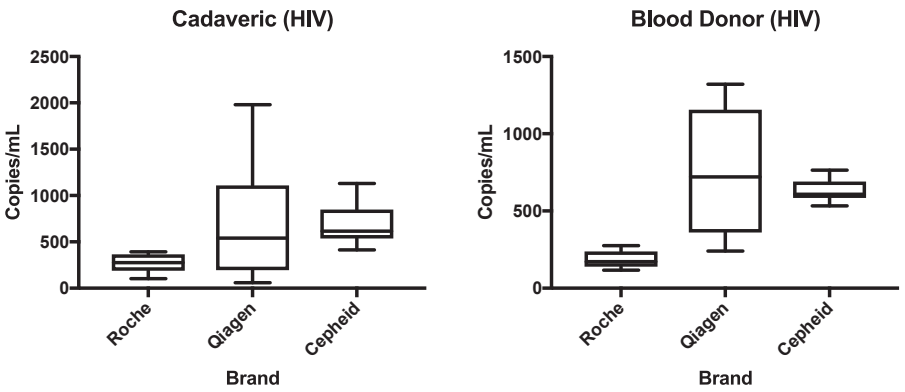

Fig. 2. Boxplot indicating HIV (copies/ml) mean detection and SD among the brands for cadaveric and blood donor samples by Student's *t*-test. For CD group (left), all spiked samples were included (n = 20) for each test. For BD group (right), all spiked samples were included (n = 10). For CD group and for each brand, invalid results were considered as 0.

Table 1
Cohen's kappa coefficient (κ) between Cepheid, Roche and Qiagen results for HIV and HCV detection. The agreement values established are: < 0.00: Poor, 0.00-0.20: Slight, 0.21-0.40: Fair, 0.41-0.60: Moderate, 0.61-0.80: Substantial and 0.81–1.00: Almost perfect.

	HIV			HCV		
	Cohen's κ	% of agreement	Agreement	Cohen's κ	% of agreement	Agreement
Cepheid vs. Roche	0.89	97%	Almost perfect	0.80	95%	Almost perfect
Cepheid vs. Qiagen	0.13	44%	Slight	0.33	67%	Fair
Roche vs. Qiagen	0.12	43%	Slight	0.17	53%	Slight

Table 2
Results of sensitivity, specificity and accuracy of each test of each brand, respectively. Sensitivity was calculated using the total of spiked samples from cadaveric donors (n = 20), specificity was calculated using the total of non-spiked samples from cadaveric donors (n = 5) and accuaracy was calculated using the total of quantified samples divided by the total number of both spiked and non-spiked samples from cadaveric donors.

Brand	Virus	Sensitivity	Specificity	Accuracy
Cepheid	HIV	19/20, 95%	5/5, 100%	24/25, 96%
Cepheid	HCV	20/20, 100%	5/5, 100%	25/25, 100%
Roche	HIV	20/20, 100%	5/5, 100%	25/25, 100%
Roche	HCV	16/20, 80%	3/5, 60%	19/25, 76%
Qiagen	HIV	10/20, 50%	2/5, 40%	12/25, 48%
Qiagen	HCV	0/20, 0%	1/5, 20%	0/25, 0%

inability to obtain results (detectable and quantifiable) varied according to the brand and virus, but it was observed more times in Qiagen kits, which showed more invalid results than the other brands. In addition, not detected results in spiked samples were observed in Roche and Qiagen kits, but both HIV and HCV Qiagen kits showed this inaccurate result with more frequency.

Usually, qualitative NAT tests have been recommended to be used to analyze cadaveric samples, which have showed higher specificity, accuracy and sensitivity [14], detecting lower viral loads than quantitative NAT tests. In Brazil, only quantitative PCR tests are commercially available to detect these pathogens. However, this probably would not change the findings, as the results observed most likely are a consequence of the DNA/RNA purification system. The utility of the quantitative results of these assays should be interpreted, and used only for complementary screening. In the tissue banks, any inconclusive or controversial result is a subject to discharge the tissues.

This study has some limitations. (i) The samples were spiked with a viral load of 1000 copies/mL, thus, this test cannot be reliable for tests in cadaveric donor with lower viral loads. However, in the acute phase of HCV/HIV, where antibody-based tests can be negative, viral loads are extremely high, reducing this limitation [29,30]. (ii) Another point to highlight is that quantitative tests might fail in situations of elite controllers (people who have undetectable viral load even without treatment), but these cases would be detected by serological tests [31], which remain mandatory for tissue transplantation. (iii) Quantitative kits cannot be as sensitive as qualitative NAT tests. The assays we validated in this study are not used or indicated for these kinds of samples, thus, we suggest using only when specific commercial cadaveric tests are not available.

The evaluation and comparison of the different tests and brands showed that the assays have a wide variability in their ability to accurately and reliably provide results on cadaveric specimens. The Cepheid and Roche kits were more sensitive in detecting HIV/HCV on

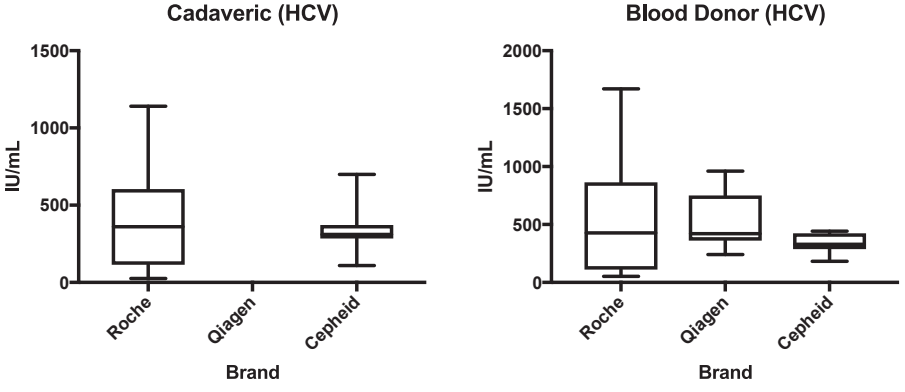

Fig. 3. Boxplot indicating HCV (IU/ml) mean detection and SD among the brands for cadaveric and blood donor samples by Student's *t*-test. For the cadaveric sample figure, the Qiagen brand was not shown due to a lack of amplification. For CD group (left), all spiked samples were included (n = 20) for each test. For BD group (right), all spiked samples were included (n = 10). For CD group and for each brand, invalid results were considered as 0.

cadaveric samples than the Qiagen kit. The Roche and Cepheid kits can be used for screening tissue donors for HIV and HCV with more than 1000 copies or IU/ml, respectively.

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CRediT authorship contribution statement

Victoria Stadler Tasca Ribeiro: Formal analysis, Writing - original draft, Methodology. **Sonia Mara Raboni:** Conceptualization, Funding acquisition, Supervision, Writing - original draft, Methodology. **Paula Hansen Suss:** Conceptualization, Funding acquisition, Project administration. **Juliette Cieslinski:** Formal analysis, Visualization. **Letícia Kraft:** Formal analysis, Visualization. **Jucélia Stadinicki dos Santos:** Supervision, Validation. **Luciane Pereira:** Supervision, Validation. **Felipe Francisco Tuon:** Conceptualization, Funding acquisition, Supervision, Writing - original draft, Methodology.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2019.104203.

References

[1] M.A. Greenwald, M.J. Kuehnert, J.A. Fishman, Infectious disease transmission during organ and tissue transplantation, Emerg. Infect. Dis. 18 (8) (2012) e1.
[2] P.A. Grossi, J.A. Fishman, Practice ASTIDCo: Donor-derived infections in solid organ transplant recipients, Am. J. Transplant. 9 (Suppl 4) (2009) S19–26.
[3] D. Guyotat, J.F. Nicolas, F. Augey, D. Fiere, J. Thivolet, Porphyria cutanea tarda after allogeneic bone marrow transplantation for chronic myelogenous leukemia, Am. J. Hematol. 34 (1) (1990) 69–70.
[4] A. Pruss, G. Caspari, D.H. Kruger, J. Blumel, C.M. Nubling, L. Gurtler, W.H. Gerlich, Tissue donation and virus safety: more nucleic acid amplification testing is needed, Transpl. Infect. Dis. 12 (5) (2010) 375–386.
[5] T.N. Victer, C.S. Dos Santos, S.N. Bao, T.L. Sampaio, Deceased tissue donor serology and molecular testing for HIV, hepatitis B and hepatitis C viruses: a lack of cadaveric validated tests, Cell Tissue Bank. 17 (4) (2016) 543–553.
[6] T. Eastlund, Infectious disease transmission through cell, tissue, and organ transplantation: reducing the risk through donor selection, Cell Transplant. 4 (5) (1995) 455–477.
[7] W.W. Tomford, Transmission of disease through transplantation of musculoskeletal allografts, J. Bone Joint Surg. Am. 77 (11) (1995) 1742–1754.
[8] E.U. Conrad, D.R. Gretch, K.R. Obermeyer, M.S. Moogk, M. Sayers, J.J. Wilson, D.M. Strong, Transmission of the hepatitis-C virus by tissue transplantation, J. Bone Joint Surg. Am. 77 (2) (1995) 214–224.
[9] J.A. Fishman, M.A. Greenwald, P.A. Grossi, Transmission of infection with human allografts: essential considerations in donor screening, Clin. Infect. Dis. 55 (5) (2012) 720–727.
[10] M.G. Ison, E. Llata, C.S. Conover, J.J. Friedewald, S.I. Gerber, A. Grigoryan, W. Heneine, J.M. Millis, D.M. Simon, C.G. Teo, et al., Transmission of human immunodeficiency virus and hepatitis C virus from an organ donor to four transplant recipients, Am. J. Transplant. 11 (6) (2011) 1218–1225.
[11] F.L. Delmonico, Cadaver donor screening for infectious agents in solid organ transplantation, Clin. Infect. Dis. 31 (3) (2000) 781–786.
[12] M.A. Greenwald, S. Kerby, K. Francis, A.C. Noller, W.T. Gormley, R. Biswas, R.A. Forshee, Detection of human immunodeficiency virus, hepatitis C virus, and hepatitis B virus in postmortem blood specimens using infectious disease assays licensed for cadaveric donor screening, Transpl. Infect. Dis. 20 (1) (2018).
[13] T. Meyer, S. Polywka, B. Wulff, C. Edler, A.S. Schroder, I. Wilkemeyer, U. Kalus, A. Pruss, Virus NAT for HIV, HBV, and HCV in post-mortal blood specimens over 48 h after death of infected patients - first results, Transfus. Med. Hemother. 39 (6) (2012) 376–380.
[14] K. Gubbe, Y. Scharnagl, S. Grosch, T. Tonn, M. Schmidt, K.M. Hourfar, A. Karl, E. Seifried, I. Wilkemeyer, U. Kalus, Validation of virus NAT for HIV, HCV, HBV and HAV using post-mortal blood samples, Transfus. Med. Hemother. 39 (6) (2012) 381–385.
[15] R. Dodd, W. Kurt Roth, P. Ashford, E.M. Dax, G. Vyas, Transfusion medicine and safety, Biologicals 37 (2) (2009) 62–70.
[16] M.H. Koppelman, H.T. Cuijpers, S. Wessberg, A. Valkeajarvi, L. Pichl, V. Schottstedt, J. Saldanha, Multicenter evaluation of a commercial multiplex polymerase chain reaction test for screening plasma donations for parvovirus B19 DNA and hepatitis A virus RNA, Transfusion 52 (7) (2012) 1498–1508.
[17] M. Vermeulen, N. Lelie, W. Sykes, R. Crookes, J. Swanevelder, L. Gaggia, M. Le Roux, E. Kuun, S. Gulube, R. Reddy, Impact of individual-donation nucleic acid testing on risk of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission by blood transfusion in South Africa, Transfusion 49 (6) (2009) 1115–1125.
[18] U. Kalus, I. Wilkemeyer, G. Caspari, J. Schroeter, A. Pruss, Validation of the Serological Testing for Anti-HIV-1/2, Anti-HCV, HBsAg, and Anti-HBc from Postmortem Blood on the Siemens-BEP-III Automatic System, Transfus. Med. Hemother. 38 (6) (2011) 365–372.
[19] ANVISA: Boas Práticas Em Tecidos Humanos Para Uso Terapêutico. Resolução RDC n55, (2015).
[20] C. Pronier, S. Boukthir, L. Courtellemont, G. Lagathu, A. Maillard, V. Thibault, Performance comparison of new Veris and Xpert random access HIV-1 RNA quantification assays, Virol. J. 15 (1) (2018) 156.
[21] B. Senechal, V.L. James, Ten years of external quality assessment of human immunodeficiency virus type 1 RNA quantification, J. Clin. Microbiol. 50 (11) (2012) 3614–3619.
[22] F.S. Nolte, Impact of viral load testing on patient care, Arch. Pathol. Lab. Med. 123 (11) (1999) 1011–1014.
[23] D.M. Strong, K. Nelson, M. Pierce, S.L. Stramer, Preventing disease transmission by deceased tissue donors by testing blood for viral nucleic acid, Cell Tissue Bank. 6 (4) (2005) 255–262.
[24] I. Wilkemeyer, A. Pruss, U. Kalus, J. Schroeter, Comparative infectious serology testing of pre- and post-mortem blood samples from cornea donors, Cell Tissue Bank. 13 (3) (2012) 447–452.
[25] A.D. Kitchen, H.L. Gillan, The serological screening of deceased tissue donors within the English Blood Service for infectious agents–a review of current outcomes and a more effective strategy for the future, Vox Sang. 98 (3 Pt 1) (2010) e193–200.
[26] A. Amendola, P. Marsella, M. Bloisi, F. Forbici, C. Angeletti, M.R. Capobianchi, Ability of two commercially available assays (Abbott RealTime HIV-1 and Roche Cobas AmpliPrep/Cobas TaqMan HIV-1 Version 2.0) to quantify low HIV-1 RNA Levels (< 1,000 copies/milliliter): comparison with clinical samples and NIBSC working reagent for nucleic acid testing assays, J. Clin. Microbiol. 52 (6) (2014) 2019–2026.
[28] D. Sizmann, C. Boeck, J. Boelter, D. Fischer, M. Miethke, S. Nicolaus, M. Zadak, R. Babiel, Fully automated quantification of hepatitis C virus (HCV) RNA in human plasma and human serum by the COBAS AmpliPrep/COBAS TaqMan system, J. Clin. Virol. 38 (4) (2007) 326–333.
[29] A.D. Kitchen, J.A. Newham, H.L. Gillan, Effective serological and molecular screening of deceased tissue donors, Cell Tissue Bank. 14 (4) (2013) 633–644.
[30] S. Zou, R.Y. Dodd, S.L. Stramer, D.M. Strong, Tissue safety study g: probability of viremia with HBV, HCV, HIV, and HTLV among tissue donors in the United States, N. Engl. J. Med. 351 (8) (2004) 751–759.
[31] K. Cilliers, C.J.F. Muller, B.J. Page, Human immunodeficiency virus in cadavers: a review, Clin. Anat. 32 (4) (2019) 603–610.