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Abstract. Metal artifacts have been a problem associated with computed tomography (CT) since its introduction. Recent techniques to mitigate this problem have included utilization of high-energy (keV) virtual monochromatic spectral (VMS) images, produced via dual-energy CT (DECT). A problem with these high-keV images is that contrast enhancement provided by all commercially available contrast media is severely reduced. Contrast agents based on higher atomic number elements can maintain contrast at the higher energy levels where artifacts are reduced. This study evaluated three such candidate elements: bismuth, tantalum, and tungsten, as well as two conventional contrast elements: iodine and barium. A water-based phantom with vials containing these five elements in solution, as well as different artifact-producing metal structures, was scanned with a DECT scanner capable of rapid operating voltage switching. In the VMS datasets, substantial reductions in the contrast were observed for iodine and barium, which suffered from contrast reductions of 97% and 91%, respectively, at 140 versus 40 keV. In comparison under the same conditions, the candidate agents demonstrated contrast enhancement reductions of only 20%, 29%, and 32% for tungsten, tantalum, and bismuth, respectively. At 140 versus 40 keV, metal artifact severity was reduced by 57% to 85% depending on the phantom configuration.

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1 Introduction

Up to 21% of computed tomography (CT) scans are degraded by radiodense metal objects, including shrapnel, surgical clips, prostheses, pacers, embolization coils, or external monitoring devices.¹ Artifact severity can range from slight, localized image artifacts to severe, far-ranging artifacts that may obscure gross anatomy and render diagnosis impossible. The issue is compounded as the region of diagnostic interest often centers on tissues around implanted metal objects; medical devices are placed in injuries and may themselves damage vessels, tissues, and bone by impact, erosion, infection, inflammation, or migration. This means that even localized artifacts are often detrimental to the diagnostic acceptability of the images.

Several metal artifact reduction methods have been developed to mitigate this problem,^{1–4} with some now in commercially available form for clinical use.^{5,6} These methods involve the identification and replacement of metal-corrupted CT data, usually in projection space through iterative techniques. While these techniques have been shown to successfully reduce metal artifacts, a current limitation with commercial metal artifact reduction software (MARS) is the possibility that it may introduce further artifacts that may lead to misinterpretation.^{7–10}

The use of virtual monochromatic spectral (VMS) images computed at high x-ray energies (90 to 140 keV) generated via dual-energy CT (DECT) has recently emerged as an important additional tool to reduce metal artifacts.^{11–15} This technique involves selection of higher energy levels than those available in

standard CT, which generates images representative of the mean energy of the x-ray beam, emphasizing the contribution from more penetrating x-rays, minimizing artifacts from both metal and beam hardening. Furthermore, VMS images do not produce the tissue distortion that might occur using commercial MARS because the projection data are not manipulated in the same way.

A problem associated with high-keV images, where metal artifacts are diminished, is a reduction in the contrast agent signal from iodine and barium that is needed for vascular and soft tissue diagnoses.¹⁶ The contrast agent signal is higher at the lower VMS levels and decreases with increasing energy level; at higher energy levels, the contrast signal may be completely lost (Fig. 1).¹⁷ This signal loss is intrinsic to iodine or barium as the reporter element since these elements have *k* edges of 33 and 37 keV, respectively. These relatively low-energy *k* edges, which result in a step increase in x-ray attenuation at that characteristic energy level, provide acceptable image contrast for single-energy CT with its mean x-ray energy of ~66 keV at 120 kVp¹⁸ but are associated with a substantially reduced attenuation at higher keV levels. Elements with *k* edges at higher x-ray energies are, therefore, attractive for use with DECT; their x-ray attenuation is greater at the desired higher keV levels, provided their *k* edges are near the effective x-ray spectrum's mean energy. Contrast enhancement begins to diminish for elements with *k* edge energy levels above the effective x-ray spectrum's mean energy. Nevertheless, for many high-Z elements, contrast enhancement still exceeds that of iodine in the higher keV range.¹⁹

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Fig. 1 Dual-energy computed tomography (DECT) imaging with conventional contrast agents. (a) A nasogastric tube (arrowheads) is producing a significant metal artifact, obscuring the gastric wall in a contrast-enhanced DECT abdomen virtual monochromatic spectral (VMS) image generated at 65 keV. (b) While reduced metal artifact is seen at 100 keV, the contrast enhancement is also markedly diminished (arrows), thereby rendering this image nearly useless for the evaluation of blood vessels and enhancement of the stomach wall.

Table 1 Specification of the contrast elements.

Element	Atomic number (Z)	<i>k</i> edge	Compound used	Concentration of contrast element (mg/mL)	Chemical formula
Iodine	53	33.2	Iohexol	10.2	C ₁₉ H ₂₆ I ₃ N ₃ O ₉
Barium	56	37.4	Barium sulphate	9.8	BaSO ₄
Tantalum	73	67.4	Tantalum oxide	10.1	Ta ₂ O ₅
Tungsten	74	69.5	Sodium tungsten dihydrate	12.2	Na ₂ WO ₄ · 2H ₂ O
Bismuth	83	90.5	Bismuth citrate	13.7	C ₆ H ₅ BiO ₇

High-keV images without contrast enhancement are of limited diagnostic use for many CT indications including detection of active bleeding near shrapnel or recent postsurgical sites, vascular stenosis or aneurysms near metal implants or embolization coils, or the presence of infection or soft tissue injury, which frequently occur near metallic foreign bodies.^{20,21} All commercially available CT contrast agents for routine clinical use employ either iodine or barium as the reporter element.

The aim of this study was to evaluate a representative selection (Table 1) of conventional and novel CT contrast elements either in development^{22–25} or in routine clinical use. The near-threefold difference in *k* edge energy between different elements was anticipated to result in widely varying attenuation profiles over the 40 to 140 keV range. Candidate elements capable of producing images with simultaneous high contrast enhancement and low metal artifact could thus be identified. These materials were imaged in a range of different phantom configurations, with varying metal artifact type and phantom size, in order to generate a more comprehensive understanding of the behavior of these elements.

2 Methodology

2.1 Phantoms

An acrylic cylinder, 203 mm in diameter and 150 mm in depth, was used as the housing for the phantom. Plastic vials, 26 mm in diameter providing a volume of 50 mL, were used to contain the contrast media, details of which are given in Table 1.

The contrast vials were mounted in a circular pattern in the phantom, which was then filled with water. Contrast elements were formulated in aqueous solutions where possible or else were kept in suspension using 1% methyl cellulose to maintain a uniform distribution within the vial. The concentrations of the compounds were chosen to provide 300 HU enhancement at 120 kVp single-energy CT.

Two types of metal implants were used in separate phantom configurations to produce different artifact types. The first configuration used ten 316-grade surgical stainless steel rods, 3 mm in diameter, with two rods attached along the length of each vial to produce uniform artifacts along the *z*-axis and transaxially through each contrast vial. The second configuration used a single-femoral head implant mounted in the center of the phantom, again producing uniform artifacts through each contrast vial. The femoral head implant was composed of a cobalt–chromium–molybdenum alloy, 42 mm in diameter at its widest point. All vials and implants were mounted using moldable polycaprolactone plastic fixtures, which produces a CT number of 40 HU at 120 kVp and thus, does not produce additional artifacts.

Four different fat encasement configurations were used to simulate larger patient sizes. These encasements were constructed using heat-sealed polyethylene bags filled with semi-solid vegetable fat, with a CT number of –105 HU at 120 kVp. The four different encasement configurations gave equivalent patient diameters of 241, 274, 301 and 323 mm, which, in addition to the 203-mm base phantom, provided simulated patient

Fig. 2 Axial 140 keV VMS CT images showing the different size fat encasements with equivalent diameters of (a) 241 mm, (b) 274 mm, (c) 301 mm, and (d) 323 mm. The region of interest (ROI) used for artifact severity calculation is shown in yellow in (a).

girths ranging from 25 in. to 40 in. Due to their semisolid nature, the encasements resulted in a more trapezoidal shape, which more realistically represent patients (Fig. 2).

2.2 Computed Tomography Imaging

CT imaging was performed using a Discovery CT750HD™ (GE Healthcare, Little Chalfont, United Kingdom) fast kVp switching DECT scanner. The protocol consisted of rapidly switching between 80 and 140 kVp on alternating projections during a single gantry rotation, and using a helical pitch of 1.375, a full-beam collimation of 40 mm (0.625 mm × 64 detector rows), a large bowtie filter, and a rotation time and tube current dependent on the radiation exposure required. For each phantom configuration, an attempt was made to match the CTDIvol to that prescribed for a single-energy scan, based on the localizer radiograph. This was possible for the three largest phantom sizes [Figs. 2(b)–2(d)]; however, the minimum dose limit of the dual-energy protocols was reached for the two smallest phantom sizes. For the five phantom sizes, the corresponding CTDIvols were, therefore, in ascending size order, 6.48, 6.48, 6.52, 10.76, and 15.65 mGy. All images were reconstructed at the thickness of 2.5 mm and a display field of view of 500 mm. Reconstructed images were processed using the Advantage Workstation 2 software (GE Healthcare). VMS datasets ranging from 40 to 140 keV were analyzed in 10 keV increments, with an additional 65 keV series generated to simulate a 120 kVp single-energy scan. All VMS datasets were additionally reconstructed with the MARS activated.

2.3 Image Analysis

The CT number (HU) of each contrast vial was recorded from each VMS dataset using oval 1.5 cm² regions of interest (ROI) in four axial images near the front face of the phantom where metal artifacts were not present. Background image noise was also recorded from the same axial images using circular 28 cm² ROIs placed in water. In each case, the mean of the four measurements was taken. Metal artifact severity was assessed with an annular ROI of 70 mm in diameter and 5 voxels (4.88 mm) in

width, placed in the center of the phantom in all axes, corresponding to the region where artifacts were most severe [Fig. 2(a)]. This ROI area contained only water in all datasets and was applied to all phantom configurations. Artifact severity was measured as the standard deviation (SD) of the CT number within this ROI. To evaluate the influence of the different phantom sizes, for each equivalent phantom diameter, the artifact severity was measured in the 65 keV dataset using the method above using the same ROI location.

3 Results

3.1 Contrast Material Performance

The mass concentrations of the reporter elements required to reach 300 HU at 120 kVp ranged from 9.8 mg/mL for barium to 13.7 mg/mL for bismuth (Table 1). This is contrary to the expected result of decreasing concentration (increasing image contrast/concentration) with increasing Z. This result must be treated with caution, however, due to the lack of consideration of the structural form of the element, the presence of other elements in the compound, and their combined effect on attenuation. The conventional elements used in clinical practice showed the highest loss of contrast signal with increasing energy over the 40 to 140 keV range, with percentage decreases in the CT number of 97% for iodine and 91% for barium for the 140-keV HU value relative to the 40-keV HU value (Fig. 3). The novel candidate agents displayed more consistent contrast enhancement across the VMS energy range, with a CT number reductions of 21%, 29%, and 32% for tungsten, tantalum, and bismuth, respectively. The *k* edge absorption discontinuities of the high atomic number (high Z) materials are not visible; the decomposition of the low- and high-energy projection data sets used to generate the basis material images, which are then combined to generate the VMS images, did not use a basis material comprising one of the contrast elements. The intersection between all the results at ~65 keV and ~300 HU reflects our choice to formulate the different contrast materials' concentrations to produce 300 HU at 120 kVp single-energy CT.

The VMS contrast performance of the different elements was consistent over the range of phantom sizes evaluated, with results from selected conventional and novel materials (iodine and tungsten) shown graphically (Fig. 4). For the smallest phantom size, iodine lost 92% of its contrast signal from 65 to

Fig. 3 Line plot showing the variation in contrast signal for the different elements over the 40 to 140 keV range, using the baseline phantom without fast encasement.

Fig. 4 Line plot showing the effect of the phantom size on the 65 and 140 keV VMS images for selected conventional and novel contrast elements: iodine and tungsten, respectively.

140 keV, whereas at the largest phantom size, the signal loss was 88%. For tungsten, the same measurements were 7% and 3% decreases for the smallest and largest phantom sizes, respectively. These trends were typical of the five elements studied.

3.2 Artifact Evaluation

For the 203-mm diameter phantom in the rod configuration, the artifact severity decreased by 85% at 140 versus 40 keV from a SD of 223 HU at 40 keV to 34 HU at 140 keV (Fig. 5). With MARS activated, this decrease was 63%, from 96 to 35 HU. In the femoral head configuration over the same energy range, the artifact severity decrease was 57%, from 168 to 72 HU. With MARS activated, this decrease was 60%, from 70 to 28 HU. Over the VMS range, the activation of MARS had a much more variable effect in the rod configuration, with a large effect at low keV and a negligible effect at high keV (Fig. 5). By contrast, for the femoral head, MARS produced a more consistent effect across the energy range (Fig. 5). Also of note is the non-linear artifact reduction in all four configurations, with a noticeable “heel” present at 65 keV for the rods + MARS, femoral head, and femoral head + MARS datasets. For the rods’ dataset alone, the reduction was slightly more linear, with a less

Fig. 5 Line plot showing the variation in metal artifact severity over the 40 to 140 keV monochromatic energy range for the two different phantom configurations (femoral head and rod) and datasets [without and with metal artifact reduction software (MARS)], using the baseline phantom without fat encasement.

pronounced “heel” present at an energy level of 80 keV (Fig. 5). The addition of MARS had no effect on the background image noise, with equal SD values in the water ROI without and with MARS in all datasets.

We observe the most successful metal artifact reduction at energies where the conventional contrast agents containing iodine and barium produced very low contrast signal, whereas the high-Z elements maintained consistent contrast signal at these energies [Figs. 6(c), 6(f), and 7). The elements’ nonlinear attenuation curves (Fig. 3) combined with the nonlinear artifact severity curves (Fig. 5), produce near-linear trends for CT number versus artifact severity (Fig. 7). As in Fig. 3, a flatter gradient is observed for the representative novel agent tungsten, which compared to iodine provides higher CT numbers in the low artifact severity region. Apparent in the CT images is the trend of greater artifact reduction between the 65 to 140 keV images for the rod configuration [Figs. 6(b) and 6(c)] compared to the femoral head configuration [Figs. 6(e) and 6(f)], where the artifacts appear similar to each other.

In the rod configuration, the MARS datasets displayed smoother artifact gradients, thus reducing the streak artifacts induced by the rods (Figs. 8(a) and 8(b)). This is expected because signals in the detector suffering from signal starvation (low incident x-ray flux) are algorithmically adjusted to improve the fidelity of the resulting reconstruction. In the femoral head configuration, due to the large, single, spatially smooth, artifact-producing object, the streak artifacts were less severe; the high-frequency artifact texture was reduced by MARS, while the low-frequency artifact pattern and fidelity of the image objects remained similar to each other [Figs. 8(c) and 8(d)].

Figure 9 shows the artifact severity versus phantom diameter measured at 65 keV. For both phantom configurations, the artifact severity remains similar across the size range, with the addition of MARS universally reducing this severity by a factor of ~ 2 . However, the data appears imprecise, no obvious trend in artifact severity with phantom size is observed, and our ability to reach statistically significant conclusions about this result is limited by statistical uncertainty or perhaps by the method that we chose. A potential source of error is the dependency of mean photon energy on phantom size.¹⁸ A fixed VMS energy of 65 keV was used across all phantom configurations, since measuring the mean photon energy at different phantom sizes was not within the scope of the study. An increase in mean photon energy with increasing phantom size would be expected and not accounting for this increase may have affected the results in Fig. 9.

4 Discussion

The first major finding of the work was the improved performance of the candidate high-Z contrast elements at the high energy levels for VMS images where metal artifacts were minimized. This demonstrates an unexplored benefit that these materials may offer, in addition to lower toxicity, lower required concentration, and prolonged circulation time.^{26,27}

The second major finding of the study was the change in artifact severity, appearance, and response to MARS, observed between different metal implant types. The configuration of five groups of rods produced a high-frequency streak pattern artifact that was greatly reduced (by 85%) at high keV and was altered with the application of MARS. The single-femoral head produced a lower frequency distortion artifact that was less significantly reduced (by 57%) at high keV and was not altered

Fig. 6 Axial VMS CT images showing metal artifact detail and contrast agent enhancement in the two phantom configurations (all images window = 400 and level = 0): (a) rods at 40 keV, (b) rods at 65 keV, (c) rods at 140 keV, (d) femoral head at 40 keV, (e) femoral head at 65 keV, and (f) femoral head at 140 keV. A similar trend in contrast enhancement loss between conventional and novel elements is present in the two configurations (c) and (f). Images were generated without MARS.

Fig. 7 Line plot showing the contrast signal for selected conventional and novel contrast elements versus metal artifact severity, measured using the baseline phantom without fat encasement in the rod configuration. The data points for each element represent the different VMS levels over the 40 to 140 keV range. Superior contrast signal is maintained at the lowest artifact severities for tungsten compared to iodine, both without and with MARS. Trends are typical of the five elements studied.

in terms of its pattern with the application of MARS. This finding suggests that for multiple small metal objects, monochromatic high-keV images are very beneficial to image quality. However, MARS should be used with caution for this artifact type due to incomplete restoration of image quality to levels achievable in the absence of metal structures, which may lead to misdiagnosis of pathology such as internal bleeding. For a single large implant such as a hip prosthesis, a combination of selected high-keV VMS images and MARS application is recommended to minimize artifacts. This finding is in agreement with previous research that has shown MARS to be most effective for artifacts generated by large metal prostheses.⁷

Fig. 8 Axial VMS CT images at 65 keV showing the effect of the MARS: (a) rods without MARS, (b) rods with MARS, (c) femoral head without MARS, and (d) femoral head with MARS.

The third major finding was the consistent contrast enhancement of the different elements over the range of phantom sizes evaluated. In single-energy CT, low-energy photons are preferentially absorbed, hardening the beam and reducing the image contrast provided by the contrast medium. Although corrections are applied in the reconstruction process that minimize this effect for most biological tissues, it remains pronounced for low-Z contrast materials at large patient sizes due to the increased patient path lengths and consequently reduced mass attenuation coefficient at the higher energies that are predominant in the

Fig. 9 Line plot showing the effect of the phantom size on artifact severity for 65-keV VMS images.

hardened x-ray spectrum. Lower enhancement values of contrast material are, therefore, observed for increasing phantom diameters at single-energy CT.²⁸ However, monochromatic x-ray beams are not hardened, so in theory, the attenuation coefficients in VMS images are independent of the path length through the phantom or patient.¹⁷ Consistent with theory, the CT numbers we observed for all contrast media were independent of phantom size.

As with any new drug, a novel, noniodinated contrast agent would require rigorous biological safety evaluation before being approved for clinical use. This is particularly challenging for CT contrast agents because relatively high quantities of a foreign metal, in the range of tens of grams, need to be injected directly into the vascular system.²⁹ Bismuth has been identified as a potentially suitable candidate due to its low cost and high x-ray attenuation.²⁶ Longstanding toxicity concerns with bismuth salts³⁰ can be potentially avoided by the use of coated bismuth sulphide nanoparticles. These have been administered in a murine model and have shown promising results, with high image contrast and a reported safety profile similar to existing iodinated agents.^{25,31} Siloxane-coated tantalum oxide nanoparticles have also been identified as having strong potential as future contrast media due to their contrast properties and biocompatibility.²⁶ Preclinical murine data has shown superior imaging performance, encouraging physicochemical properties, and low retention levels.^{22,24} Although the biological properties of tungsten are less well understood, tungsten agents have also been identified as potential CT contrast agents and were used in preclinical DECT imaging.^{23,32} Other high-Z elements with potential as possible CT contrast agents include gold,^{33,34} ytterbium,³⁵ and gadolinium.³⁶ In the interest of simplicity, these elements were not considered in the current study; but based on our consistent findings for the high-Z elements we tested and the increased image contrast compared to iodine at higher energies for other high-Z elements,¹⁹ one would expect that they, too, would exhibit the characteristic of contrast retention at high-keV levels compared to iodine in VMS images at higher energy levels.

One important consideration of a new contrast element is its performance at material decomposition—a key component of DECT. This technique uses low- and high-kVp projection data to estimate the relative concentration of two basis materials. This processing has valuable clinical uses such as the elimination of noncontrast scans in multiphase protocols by reconstructing

“virtual noncontrast” images, and for assessment of hemorrhage, iron quantification, and renal stone classification.^{37,38}

Iodine is readily separable from soft tissue using this technique due to the energy dependence of the differing attenuation mechanisms (photoelectric absorption versus Compton scattering) between the low- and high-energy spectra. However, iodine’s attenuation coefficient is somewhat similar to that of bone; as a result, bone and iodine are indistinguishable at some concentrations. In comparison, the attenuation coefficients of the high-Z elements are substantially different from both soft tissue and bone; the use of contrast agents containing these elements, together with new material decomposition algorithms optimized for these elements, may improve the separability of contrast-enhanced vasculature from both soft tissue and bone. Furthermore, the relative attenuation of the high-Z elements is substantially different from that of iodine, which would allow material decomposition to distinguish the signal of high-Z elements from that of iodine.^{38,39} It has been shown pre-clinically that tungsten and bismuth are separable from soft tissue and also separable from iodinated contrast material, due to their different attenuation ratios.^{23,40} This enables the possibility of double-contrast material decomposition where, for example, an iodinated agent is administered simultaneously with a high-Z agent in a different anatomical compartment. Potentially powerful clinical applications of double-contrast material decomposition could be developed, including tasks where simultaneous bowel wall and vascular enhancement are required in the abdomen²³ and for trauma imaging.⁴⁰ Projection-based material decomposition techniques may enhance the decomposition process due to the reduction (ideally, elimination) of beam hardening in the basis material density images which are used to generate the VMS images.

The combined use of VMS images and material decomposition techniques may also offer an alternative solution for contrast retention at high keV. Since the contrast material signal is potentially separable through decomposition, this signal could then be added to the high-keV VMS image to provide a further synthesized image with the benefits of both DECT techniques. New methodologies for noise suppression in the decomposition process are in development, both in projection and image space.^{41–43} In the future, with reliable material separation and improved quality in these decomposition images, blending them with VMS data may offer a viable alternative to the use of high-Z contrast agents for this task. However, the material decomposition data, which for iodine is highly dependent on the low-kVp projection data, will likely be subject to metal artifacts such as those discussed in this report. Although it may be possible to suppress statistical noise in the material decomposition process, it seems less likely that it will be possible to suppress structured errors such as metal artifacts and that DECT will still benefit from the use of a contrast agent that incorporates a high-Z element.

The study had several limitations. First, imaging was performed using a single scanner model. The use of a different DECT platform, such as a dual-source scanner, could potentially produce different results. Results could be affected by the differences in high- and low-kVp spectra employed by the two DECT approaches, by differences in dual-energy technology (i.e., fast switching versus dual-source), as a result of different VMS software, and different MARS algorithms. Second, because a static phantom was used, advantages of one technology versus another could not be evaluated regarding the efficacy

of the method in the presence of motion. In other words, the superior temporal correlation between high- and low-energy projection measurements enabled by fast kVp switching DECT technology relative to dual-source DECT technology may produce better metal artifact reduction in scans where motion is a factor. Third, the contrast elements evaluated were simple compounds, unrealistic for clinical use. The attenuation of the other low-Z elements present in each compound was neither factored into any analysis performed nor was the concentration required to reach the CT number of 300 HU. The main aim of this study was to compare the contrast profiles of the different elements, and as such, a detailed analysis of the composition and concentration was not a priority and has been performed rigorously elsewhere.¹⁹ Fourth, the semisolid nature of the fat encasements did not allow for perfect repeatability between different setups, so the precision of those datasets is likely to be lower than for the initial 203-mm diameter phantom configuration. Fifth, a control phantom without artifact-producing metal implants was not imaged. As a result, it is possible that the high attenuation of the contrast vials themselves may have contributed to some of the artifacts; however, these artifacts were expected to be consistent between the different phantom configurations, and thus did not affect the primary findings. Finally, no patient scans were performed, thus the findings require confirmation using animal models or clinical data.

In conclusion, novel candidate elements, such as bismuth, tantalum, and tungsten, displayed stable contrast enhancement over the 40 to 140 keV VMS range and are well suited as contrast agents for patients with metal implants where high-keV images are desirable. While metal artifact severity was reduced in high-keV images, the novel elements maintained clinically acceptable enhancement levels, whereas the contrast signal decreased by over 90% for the conventional elements iodine and barium. These results remained consistent across changes in the metal artifact type, application of commercial MARS, and variation in the phantom diameter, demonstrating a robust phenomenon that should transfer reliably to a clinical setting.

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