综述专论

高光谱成像技术在医药领域中的应用进展研究*

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摘要: 高光谱成像(hyperspectral image,HSI)技术是通过高光谱成像仪(高光谱相机)探测可见光光谱及不可见的近红外光谱(NIRS)范围内的波长,接收每个像素含有的上百个不同波段的反射信息形成三维立体图像的1种新型检测技术。HSI技术可提供丰富的光谱信息和空间信息,具有准确、实时、在线分析的优势,近年来在医药领域得到了广泛应用,未来在结合智能AI、5G、大数据区块链等先进的技术后将会发挥越来越重要的作用。本文就HSI技术在临床医学、中医学、基础医学、药学等医药领域的应用进行综述,并对其未来在医药领域的发展前景进行展望。

关键词: 高光谱成像技术;临床医学;中医学;基础医学;研究进展

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Research on application progress of hyperspectral imaging technology in medical field*

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Abstract: Hyperspectral image (HSI) technology is a new detection technology that detects the wavelength in the range of visible light spectrum and invisible near-infrared spectrum (NIRS) by hyperspectral camera, and receives the reflection information of hundreds of different bands contained in each pixel to form a three-dimensional image. HSI can provide rich spectral and spatial information, and has the advantages of accurate, real-time and in-situ. In recent years, HSI has been widely used in the field of medicine. In the future, HSI will play an increasingly important role after combining advanced technologies such as intelligent AI, 5 G and big data block-chain. This paper reviewed the application of HSI technology in clinical medicine, traditional Chinese

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medicine, pre-clinical medicine, pharmacy and other medical fields, and prospects its future development in the field of medicine.

Keywords: hyperspectral imaging technology; clinical medicine; traditional Chinese medicine; preclinical medicine; research progress

随着科学技术的迅速发展,医疗水平的逐渐提高,国民对健康期望值的不断提升,对医学检测的准确化、快速化、灵敏化、智能化程度等的要求也越来越高。理化检验、超声、X 射线、电子计算机断层扫描(CT)、磁共振成像(MRI)等常规传统影像学检查虽然具有较好的诊断参考价值,但会给患者身体带来一定程度的损伤,如电离电磁辐射,可能给患者带来二次创伤。而正电子发射计算机断层显像(PET-CT)虽然具有特异性、安全性高,全身显像的特点,但是因其检查费用过高,较难被普通患者群所接受。在药物分析方面,重量分析法、酸碱滴定法、pH 值测定法、电泳法、色谱、质谱检测等虽然准确性较好,但也在不同程度上存在一定的局限性,如质谱检测中气相色谱-质谱(GC-MS)法分析对糖类、苯类等不易电离的化合物响应弱,流动相只能局限于易挥发成分。液相色谱-质谱(LC-MS)法分析的样品最好是水溶液或甲醇溶液,LC 流动相中不应含不挥发盐。甚至对质谱检测器的使用方法、后期维护、操作规范等都有很高的要求,现阶段很难大范围全面铺开。高光谱成像(hyperspectral image, HSI)技术作为 1 种新兴分析手段,近年来在地质勘测、土壤植被生态监测、海洋检测、食品安全、考古文博等方面已取得了丰富的研究成果[1]。HSI 技术是将丰富的光谱信息和图像信息合并形成二维空间图像数据与一维光谱数据结合的三维信息,具有定时、定位、简便、智能、准确的特点,被大量应用在现代医学疾病的早期筛查及诊断、临床指导治疗、临床疗效评估方面,样本采集信息时间不到 10 s,几乎可以做到"实时"应用。在传统医学(中医)方面,望闻问切四诊中的望诊,作为中医诊断中的关键一步,是对病人的神、色、形、态、舌象等进行观察,判断脏腑病变。医者多年的行医经验使得诊断更为准确,这种经验难以描述、量化,一直被西医诟病[2]。而 HSI 技术的出现,并结合人工智能和深度学习技术后,将中医主观的望诊转换为可量化的数据处理、匹配及诊断过程,大大提高了望诊的准确度及可信度。除此之外,HSI 技术在法医学鉴定,组织病理分析,中药材质量控制、来源鉴别等多个领域,呈现出井喷式的发展(表 1)。

1 HSI 技术在临床医学中的应用

1.1 HSI 技术应用于临床疾病早期筛查及诊断　疾病的发生发展是 1 个极其复杂的过程,较难被察觉,HSI 技术作为 1 种"图谱合一"的三维检测技术,能够对研究对象进行数据采集,捕获更加全面的信息,同时将采集的数据处理后得到可视化的结果(如图 1)。研究者利用 HSI 技术获取外部血管血流时间及斑块的图像,成功识别了外部血管的动脉粥样硬化斑块病变,为准确治疗动脉粥样硬化疾病提供了理论依据[1]。另有相关文献指出,通过 HSI 技术捕获不同病灶的不同波段的光谱信息并加以分析,可使外周动脉疾病、下肢静脉曲张等血管性病变、关节炎[3-4],喉部疾病[5]、龋齿[6]、糖尿病病变[7]、视网膜早期病变[8-9]、不同程度皮肤损伤[10-13]、血管形态结构异常[14]等疾病的诊断更加形象具体。此外,HSI 技术基于较高的空间分辨率和光谱分辨率的特点,在肿瘤的筛查和诊断方面独具优势。目前已实现对于宫颈癌、乳腺癌、肺腺癌、胃癌、结直肠癌、舌癌、黑色素瘤、皮肤肿瘤、脑癌、口腔癌、淋巴癌、前列腺癌、卵巢癌等[15-23]的准确诊断。

1.2 HSI 技术应用于指导临床治疗　HSI 技术结合传统的临床诊疗技术,可使疾病诊断更加准确,从而提高疾病的治疗效果[24]。在肿瘤治疗过程中,HSI 技术可辅助传统诊疗设备,提高肿瘤识别率及分类性能,追踪肿瘤体内物质变化,提高肿瘤手术切除的敏感度、特异度和精确度[25]。在临床上应用 HSI 技术可检测到肿瘤微血管血流量的变化以及体内氧合血红蛋白的含量变化,区分癌组织和非癌组织[26],使得临床治疗更加精准化。此外,HSI 技术还可提供术区的可视化,便于诊疗人员高效完成高难度手术,从而减少术后并发症的发生。检测到肉眼无法观察到的组织,增强其可视化程度,提供实时信息,手术过程中利用 HSI 技术可准确找出具体施术部位,有效的避免对周围组织的损伤,确保安全高效完成手术[27-31]。

表 1　HSI 技术在医药领域的应用

Tab. 1　Application of hyperspectral-imaging technology in medical field

类别 (category)	应用范围 (scope of application)	参考文献 (reference)
临床医学 (clinical medicine)	血管病变-外周动脉及冠状动脉疾病(vascular disease-peripheral arterial disease and coronary artery disease),关节炎(arthritis),视网膜、大脑、肾脏疾病(retinal, brain and kidney disease),术中组织器官及神经纤维识别(intraoperative identification of tissues, organs and nerve fibers)	1,33-34,2-3,8-9,30-31
	龋齿(dental caries),喉部病变(laryngeal lesions),眼科疾病-视网膜病变(ophthalmic diseases-retinopathy),皮肤损伤-烧伤(skin injury-thermalinjury)	6-7,8-9,10-13
	糖尿病并发症-糖尿病足(diabetic disease-diabitic foot),肠缺血(intestinal ischemia),出血性休克(hemorrhagic shock),肾移植术(renal transplantation),肝脏切除术(hepatectomy),高脂血症(hyperlipoidemia)	27,32,33,34,42
	脑肿瘤(brain tumors),脑癌(brain cancer),肺腺癌(lung adenocarcinoma),舌癌(tongue cancer),乳腺癌(breast cancer),胃癌(gastric cancer),结直肠癌(colorectal cancer),宫颈肿瘤(cervical tumors),宫颈癌(cervical cancer),黑色素瘤(melanoma),皮肤癌(skin cancer),前列腺癌(prostate cancer),卵巢癌(ovarian cancer),淋巴癌(lymph cancer)等	16,17-23
中医学(traditional Chinese medicine)	表证(superficies syndrome),里证(interior syndrome),寒证(cold syndrome),热证(heat syndrome),虚证(deficiency syndrome),实证(sthenic syndrome),阴证(yin syndrome),阳证(yang syndrome),脏腑病症(viscera disease)[如心病(heart disease),肺热病(lung heat disease),中风(stroke)等] 针灸理疗(acupuncture-therapy)	37,38,39,40,41,43,44
基础医学-法医学及组织病理学(basic medical sciences as well as forensic and histopathology)	生物样本鉴定(identification of biological samples),血液(blood),唾液(saliva),精液(sperm),尿液(urine),组织病理切片分析(histopathological section analysis) 细胞微小病变诊断(diagnosis of microcellular lesions)	45-47,48-52
药物及其有毒有害残留物(drugs and toxic and harmful residues)	防己(Radix Stephaniae Tetrandrae),茴香(*Foeniculum vulgare Mill.*),麦冬(Radix Ophiopogonis),苦杏仁(Semen Armeniacae Amarum),桃仁(peach seed),金银花(Flos Lonicerae),人参(Ginseng Radix et Rhizoma),冬虫夏草(*Cordyceps sinensis*),枇杷叶(Folium Eriobotryae),银杏叶(*Ginkgo biloba*),桑葚(mulberry),黑枸杞(*Lycium ruthenicum*),制剂中成药(preparation of proprietary Chinese medicine),药材中农药及重金属残留(residues of pesticides and heavy metals in medicinal materials)	53-62,63-66

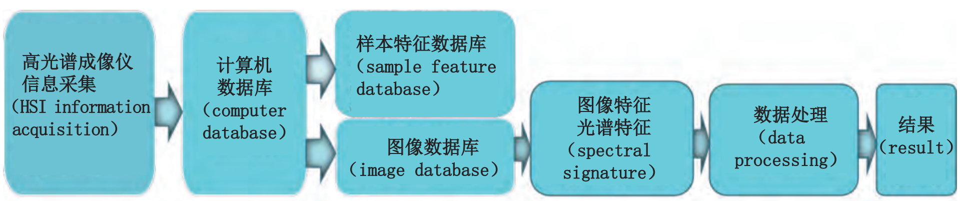

图 1　HSI 技术数据分析流程图

Fig. 1　Analysis flow of HSI technology

1.3　HSI 技术应用于临床疗效评估　HSI 技术除了指导临床治疗,还可准确评估患者治疗效果和愈后情况。相关研究发现,利用 HSI 技术能较准确的预测糖尿病的并发症(如视网膜病变、糖尿病足、糖尿病肾病等)[32]、不同程度的皮肤病变,面部及手部病变、外周动脉及冠状动脉病变[33-34]、喉部黏膜病变[35]等不同疾病的治疗效果。另外,HSI 技术还可通过检测肿瘤血管血流速率及血管程度,评估临床上联合使用与单独使用靶向药对肿瘤微血管、血管恢复、Caki-2 肿瘤的治疗效果[36]。随着 HSI 技术的发展,其研究对象将逐渐扩大化,由单一的外在器官组织扩展到复杂的内在脏器及血管;采集到的更加全面、实用的三

维数据使诊疗过程更为直观。

2 HSI 技术在中医学中的应用

2.1 HSI 技术应用于望诊 望、闻、问、切是中医诊断的 4 种传统诊断方法。但由于望诊存在主观意识性,相关研究鲜有报道。随着 HSI 技术发展,临床可运用 HSI 技术对舌裂及舌下静脉的光谱特征进行区分[37],对舌体信息进行定量化[38],收集舌色、苔色、舌苔面积信息[39],获取舌部特异性指标群[40],并结合中医中“舌通过经络与五脏六腑相连,当人体脏腑、气血、津液发生变化时,也会通过舌头反映出来”的原理来判断身体病症(如图 2)。临床上通过 HSI 技术对舌的高光谱图像和光谱特征客观的分析结合传统中医的相关知识,可以明确疾病(八纲辨病及脏腑、三焦辨病)的证型,制定合理治疗方案,准确评估疾病的转归[41]。与此同时,有文献记录[42],可通过 HSI 技术分析人类面部特征(主要指面色)的反射光谱,依据光谱曲线了解人体胆固醇含量,进一步指导高脂血症的预防和治疗。随着 HSI 技术在中医望诊的运用,相信未来 HSI 技术将通过分析患者的脉搏,声音及分泌物等的三维数据情况并结合中医整体观念和辨证论治的思想,实现四诊诊病。真正做到既病防变,未病先防,为中医的特色治疗提供了一种全新思路。

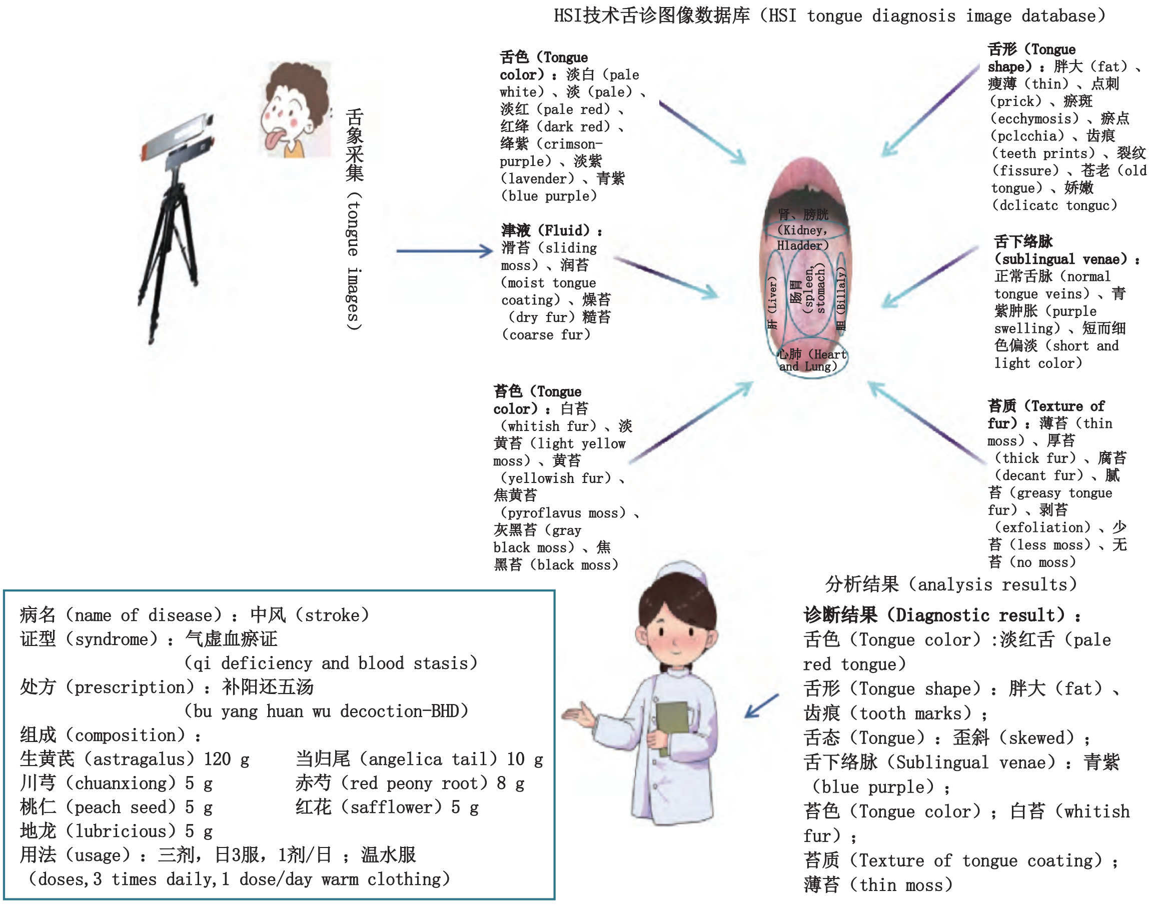

图 2 基于 HSI 技术的中医舌诊诊疗流程

Fig. 2 Tongue diagnosis and treatment process based on HSI technology

2.2 HSI 技术应用于针灸及拔罐治疗 随着国家对中医药发展的支持,越来越多的人开始相信我们几千年积淀下来的传统医学,其中部分患者更加注重通过针灸、拔罐等物理疗法来达到机体的阴平阳秘。研究发现,通过 HSI 技术观察针刺、艾灸理疗后人体腧穴内关穴区皮肤光谱曲线变化,了解针灸的治疗效果,对研究临床针灸效应有较高指导意义[43],而且利用 HSI 技术还可对拔罐前后的皮肤颜色进行定量分析[44],为临床有效拔罐提供依据,推动中医针灸理疗的发展进步。

3 HSI 技术在法医学及病理学中的应用

近年来,HSI 技术在法医学方面的研究独树一

帜,在犯罪现场,生物样本(如血液、唾液、精液、尿液等)的鉴定常常是刑事调查的关键。目前的识别样本的方法具有一定的破坏性,影响后续样本DNA的采样,为了减少法医实验室的工作量,并迅速为调查人员提供与案件相关的有价值的信息,HSI技术作为1种非侵入、快速化、无损害的新兴检测技术已实现在血迹指纹识别及痕迹鉴定等方面的应用。相关研究发现,利用HSI技术能迅速实现对指纹污染物(血迹和类似血迹的相关物质[45-47])的阳性鉴别,并根据相关检测信息,快速确定血液的身份,这对需要24 h内起诉嫌疑人的案件或现场有大量可疑血液证据的案件尤其有利[48]。其中Payne等[49]基于HSI技术的特征,成功区分纯血和胆红素血的差异并据此对患处瘀青老化程度进行对比分析,为家庭暴力及儿童虐待案件[50]的侦破提供了重要证据。此外,HSI技术作为1个强大的新兴检测工具,对于潜在痕迹[51]完全可以做到痕迹信息的定量化,对于公安机关案件的侦破有极大的帮助。另外,在病理学方面,相关文献研究表明[52],临床上利用HSI技术高分辨率的特点,对病理切片、细胞等微小病变进行定量分析,有利于疾病的诊断和评估治疗过程中药物的实际疗效。

4　HSI技术在药学领域的应用

4.1　HSI技术应用于中药材来源鉴别及质量控制　鉴别中药材真伪优劣问题是关系到中医药发展和国民健康的重要问题。传统的经验鉴别存在很大的不确定性及主观性,而HSI技术在鉴别中药材性状及来源、品质鉴别、质量控制、炮制工艺等方面不仅能摒除传统经验鉴别的局限性,还能够提供更加精确直观的技术鉴别。如HSI技术根据分析不同药物的光谱特征可以高精度(95%以上)实现对广防己与粉防己、八角茴香与日本茴香[53]、麦冬[54]、苦杏仁、桃仁[55]、金银花与山银花[56]、霉变金银花[57]等的有效鉴别;它还可以对人参(亚洲人参)、西洋参、假人参和西伯利亚人参的原料和产品进行分类[58];识别地蚕、蛹虫草掺杂的冬虫夏草粉末,提高了对冬虫夏草正品的识别度[59];有效辨别甘草和黄芪2种中药饮片;实现浙贝母、菊花、白芍、金银花等中药硫熏蒸条件下质量控制和分选[60];对中药材混合物进行检测,提高药材纯度;准确降低中药掺假量;确定了地黄炮制过程的特征及其终点[61]。有研究发现,HSI技术也被运用在西药药品造假分析、高血压药、中药原材料、中成药、片剂、药效试验装置开发和桑叶农药残留量检测及残留种类等在内的各个领域[62]。

4.2　HSI技术应用于药物成分分析　药物成分在疾病的诊断、治疗、预防过程中起着关键的作用。因此对不同药物进行定性及定量分析至关重要。HSI技术不仅能够实现药物的定性分析,也能实现定量分析[63]。张德涛等[64]采用HSI技术对银杏叶总黄酮进行定量分析,实现了黄酮含量在叶片中分布的可视化,分析HSI数据结果发现不同颜色银杏叶叶片区域黄酮含量较多,其中尤以黄色银杏叶最为显著;叶柄区黄酮含量3种不同颜色的银杏叶均较少(如图3)。邹小波等[65]首先利用HSI技术提取枇杷叶中的光谱数据,实现了对枇杷叶中三萜酸的快速测定。Huang等[66]、Zhang等[67]应用HSI技术高分辨的优点测定桑葚中花青素的含量、抗氧化活性和黑枸杞中总花色苷、总黄酮和总酚类物质含量,使得测定的药材相关指标的精确度达到90%,实现了药材的优选优用。

5　展望总结

HSI技术作为1种新型的非侵入性可视化检测技术,具有操作简便、无损原位、分辨率高、适用范围广、图谱合一等多方面优点。基于此优势使得HSI技术在医学诊断、临床研究、药物检测等方面得到了广泛应用[68]。但是由于HSI技术是新兴技术,尚在设备成本,数据处理等方面存在一些改进的空间[69]。为解决数据问题,必须对数据进行压缩处理,优化算法及样品采集系统,增加图像数据库,发展1种新型图形立体叠加的数据格式[70]。至于设备成本问题,随着HSI技术的普及,高光谱成像仪市场化程度的进一步提高,设备价格也会逐渐亲民。此外,随着时代的进步及分析技术的发展,HSI技术将以其精确化、快速化、灵敏化、安全化、非接触、无损伤等优点,在医药领域的应用成为热点[68],更重要的是,HSI技术结合AI、智能学习和大数据平台后将会更加发挥出其优越性[71],尤其在结合5G等技术后,可逐渐实现患者远程无人智能诊疗,打破传统医疗受时空限制的缺点[72]。HSI技术作为新兴的医药检测技术代表,将在各个领域建立新的行业标准,同时还可能开发出新的非侵入性和快速检测人体疾病及药物研究的手段及方法。相信在未来的医药检测领域将有更广阔的应用价值。

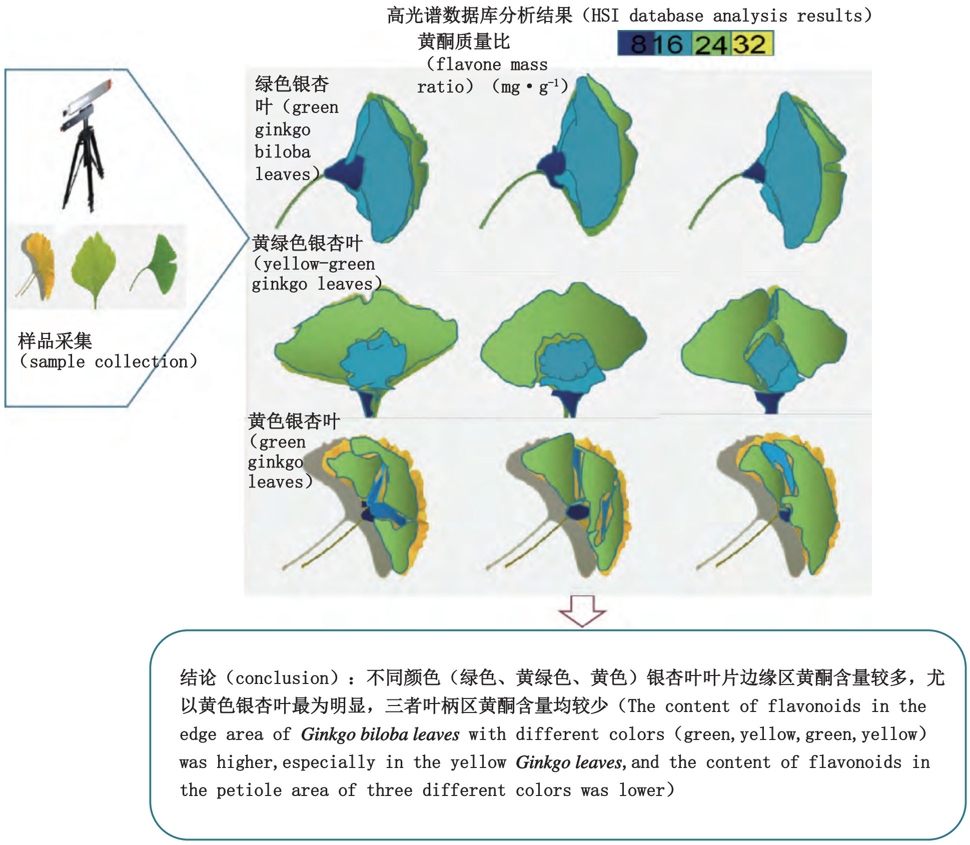

图 3　HSI 技术分析银杏叶中的黄酮含量及分布[62]

Fig. 3　The content and distribution of flavonoids in *Ginkgo biloba* leaves analyzed by HSI

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